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REACTIONS DUE TO PHENOLPHTHALEIN

A STUDY OF THEIR PATHOGENESIS

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Articles in which the harmlessness of phenolphthalein when used as a laxative has been questioned have appeared from time to time. They were concerned at first with various unexpected general symptoms and later also with the cutaneous eruptions which occur in certain persons after ingestion of the drug.

I have been investigating the action of phenolphthalein and present in this paper the results of a survey of all the available literature dealing with reactions to phenolphthalein, not only the cutaneous reactions but those consisting of general ill effects as well. The results of biochemical investigations [1] that have some bearing on the possible causes of the manifestations are also included.

REPORTS OF GENERAL REACTIONS

Incidence.—A study of the reports published in the literature since 1903 concerning cases of general disturbances attributed to the medicinal use of phenolphthalein [2] has shown that prior to 1923 the patients pre-

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1. With the technical assistance of John A. Killian, Ph.D., and Edward F. Williams Jr., Ph.D.

2. (*a*) Schwartz, O.: Der heutige Arzneimittelverkehr und dessen Einfluss auf die Krankenbehandlung, München. med. Wchnschr. **50**:24, 1903; Ueber den Gebrauch von Purgentabletten als Abführmittel bei Säuglingen und Erwachsenen, ibid. **50**:1557, 1903. (*b*) Holz, B.: Ueber Purgen-Vergiftung, Berl. klin. Wchnschr. **42**:931, 1905. (*c*) Blumenthal, F.: Diagnostische und therapeutische Vorschläge, Med. Klin. **1**:841 (July 23) 1905. (*d*) Best: Ein Fall von Purgenvergiftung, Ztschr. f. Med.-Beamte **19**:364, 1906; Näheres über Purgenvergiftung und Bemerkungen über den Arzneimittelverkehr, ibid. **19**:722, 1906. (*e*) Ortner, N.: Vorlesungen über spezielle Therapie innerer Krankheiten, ed. 4, Vienna, W. Braumüller, 1907, p. 531. (*f*) Zabel, E.: Ein Fall von Purgen-Intoxikation, Deutsche med. Wchnschr. **37**:743 (April 20) 1911. (*g*) Fontagny: Urémie et phénolphtaléine, Burgoyne méd. **8**:489, 1912. (*h*) Erdös, J.: Beitrag zur Wirk-

(Footnote continued on next page)

sented various general symptoms unaccompanied by a cutaneous eruption, whereas since 1923 several patients have also shown cutaneous manifestations of the urticarial, bullous or purpuric or the usual erythematous pigmentary type.

Hydrick in 1914 [2j] detected transient albuminuria in twenty patients after an average dose of phenolphthalein, whereas other workers [3] in a similar investigation were unable to confirm this observation. Three patients were selected in the present investigation who had albuminuria and who gave no history of intolerance to phenolphthalein. In one of these the albuminuria disappeared while in the other two it seemed to be less pronounced following the use of the drug. Two patients who had not shown any reaction to phenolphthalein presented albumi-

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ung des Purgens, Therap. Monatsh. **27**:332, 1913. (*i*) Roux, A.: Intoxication aiguë par la phénolphtaléine, Quinzaine thérapeutique, 1913, p. 179. (*j*) Hydrick, J. L.: Albuminuria Following Ingestion of Phenolphthalein, J. Biol. Chem. **17**:36, 1914. (*k*) Fürbringer: Schwere Vergiftung durch Laxativ-Drops (Phenolphthalein), Deutsche med. Wchnschr. **43**:842, 1917. (*l*) Rosenstein, P.: Der Unfug mit Phenolphthalein, München. med. Wchnschr. **67**:263, 1920. (*m*) Schmilinsky, K.: Hämolyse durch Phenolphthalein, Deutsche med. Wchnschr. **48**:1311 (Sept. 29) 1922. (*n*) Lauze, G.: Les méfaits des purgatifs synthétiques; Deux cas de purpura consécutifs à l'absorption de laxatifs à base de phénolphtaléine; traitement et guérison des accidents purpuriques par l'homohématothérapie, (injection sous-cutanée de sang humain: méthode de Sicard), Bull. Soc. d. sc. méd. et biol. de Montpellier **4**:120 (Jan.) 1923; Les méfaits des purgatifs synthétiques; deux cas de purpura consécutifs à l'absorption de phénolphtaléine; guérison par l'hémohémathérapie, Montpellier méd. **45**:260 (June 1) 1923. (*o*) Martinson, H.: "Toxic Nephritis"; Persistent Hemorrhagic Nephritis Following Ingestion of Phenolphthalein Containing Laxative, Arch. Pediat. **41**:578, 1924. (*p*) Brockelmann, E.: Drug Eruption Due to Phenolphthalein Poisoning, Bull. St. Louis Baptist Hosp. **4**:49 (Oct.) 1926. (*q*) Talley, J. E., and Glenn, H. R.: Incipient Lipoid Nephrosis and Phenolphthalein Poisoning, M. Clin. North America **13**:825 (Jan.) 1930. (*r*) Ely, R. A.: Phenolphthalein Poisoning with Analax Tablets, J. A. M. A. **98**:340 (Jan. 23) 1932. (*s*) Cleeves, M.: Poisoning by "Ex-Lax" Tablets, ibid. **99**:654 (Aug. 20) 1932. (*t*) Nelson, W. E.: Possible Phenolphthalein Poisoning, ibid. **101**:121 (July 8) 1933. (*u*) Newman, B.: Phenolphthalein Intoxication, ibid. **101**:761 (Sept. 2) 1933.

A number of references have been omitted because it was found that they contained reports of cases already cited or because they were of a general nature and gave no specific case histories. The following references could not be traced to the original source: von Jaksch, R.: Die Vergiftungen, ed, 2, Vienna, Alfred Hölder, 1910, p. 345 (Von Jaksch cited a case reported by "Wiener" in "Mündliche Mitteilung"). Devrient: Ueber die Giftigkeit des Phenolphthaleins, Kazanski M. J., October 1927 (original in Russian; not on file in this country); abstr., Schweiz. apoth. Ztg. **66**:367, 1928. This author listed several of the cases of reactions due to phenolphthalein cited in the foregoing paragraph and in addition a case reported by "Rühle" and one reported by "Alexander."

3. (*a*) Bastedo, W. A.: Materia Medica, Pharmacology and Therapeutics, ed. 3, Philadelphia, W. B. Saunders Company, 1932, p. 184. (*b*) Unterberg, E.: Beiträge zur abführenden Wirkung des Purgens, Therap. d. Gegenw. **4**:203 (May) 1902.

nuria before the use of phenolphthalein and after its use had been discontinued. Tests of sixteen different persons who showed normal chemical findings in the blood and urine prior to the taking of the drug showed no change in similar analyses made following the administration of single doses of from 0.2 to 1 Gm. of various brands of phenolphthalein. These subjects had taken phenolphthalein more than once before with no ill effects. Blood counts (not including that of the blood platelets) for seven normal subjects before and after the administration of the drug showed no significant differences in the proportion or type of the cellular elements present.

The laxative properties of phenolphthalein were discovered in 1902 by the Hungarian pharmacologist Zoltan Vámossy.[4] In the following years many clinicians stated their experiences, covering thousands of cases, with the use of this laxative without any mishap.[5] The relatively small number of reactions reported and the huge number of individual doses taken yearly [6] indicate that the untoward effects of the drug are relatively few. Some of the writers on the action of phenolphthalein, for instance, Vámossy,[7] Rowntree [8] and Wood,[9] did not believe that

4. Vámossy in a recent publication (Orvosi hetil. **78**:792 [Aug. 25] 1934) corrected the prevalent belief that the laxative action of phenolphthalein was discovered accidentally. He stated that the Hungarian government asked him to investigate the effects of phenolphthalein before using it as a denaturant of artificial wines. He did not discover the laxative effects of phenolphthalein as a result of such action in those drinking these wines but by the actual trial of the drug first on himself and then on some of his colleagues. Considering the small traces of phenolphthalein necessary for a color reaction in wine, it would have been necessary to drink as much as 10 liters of the wine in order to obtain a laxative effect.

5. (*a*) Berthoumeau, M., and Daguin, A.: Les propriétés purgatives de la phénolphtaléine, Presse méd. **16**:378, 1908. (*b*) Jarvis, G. O.: Phenolphthalein as a Purgative, Internat. M. Mag. **11**:722, 1902. (*c*) Magnus, R.: Allgemeines über Abführmittel, in Bock, J., et al.: Handbuch der experimentellen Pharmakologie, Berlin, Julius Springer, 1920, vol. 2, p. 1592. (*d*) McWalter, J. C.: One Thousand Doses of Phenolphthalein, Lancet **2**:1141 (Nov. 20) 1915. (*e*) von Noorden, C.: Zur Behandlung der Stuhlträgheit, Med. Klin. **26**:1429, 1930. (*f*) Unterberg.[3b] (*g*) Wenhardt, J.: Ueber Purgen, ein neues Abführmittel, Heilkunde, 1902, p. 212. (*h*) Wood, H. C., Jr.: The Use of Phenolphthalein as a Cathartic, Philadelphia Gen. Hosp. Rep. **7**:183, 1909. There are other reports too numerous to mention.

6. According to the figures of the United States Tariff Commission, the sales of medicinal phenolphthalein in this country amounted to 451,418 pounds (204,710 Kg.) for 1933. On the basis of the U. S. P. dose of 1 grain (0.06 Gm.), it is estimated that in America last year several billion doses of phenolphthalein were consumed.

7. Vámossy, Z.: Ueber ein neues Abführmittel (Purgen), Therap. d. Gegenw. **4**:201 (May) 1902.

8. Rowntree, L. G.: Subcutaneous Purgatives: A Clinical Study of Phenoltetrachlorphthalein (see discussion), J. A. M. A. **54**:348 (Jan. 29) 1910.

9. Wood, H. C., Jr., in discussion on Rowntree.[8]

phenolphthalein possesses any toxic qualities even when given in an overdose. Several authors, for instance, Brasch, Gillette and Kaminsky,[10] have reported on the absence of unusual symptoms in infants and children who had accidentally taken overdoses. In Orland's case [10d] the child took an overdose of 27 grains (1.75 Gm.); in addition to the diarrheal action there were slight body pains and some diminution of the urinary output that lasted for a few days; there were no other symptoms. Vámossy, in answer to the theoretical objections raised by Schwartz [2a] regarding the use of phenolphthalein in children, stated that he knew of several instances in which a 4 or 5 year old child took as many as 25 pastilles of "Baby Purgen" (1.25 Gm. of phenolphthalein) and had no ill effects aside from diarrhea. Other authors record that adults who took large doses also suffered no ill consequences. Elmer [11] reported the cases of four patients each of whom had taken 30 grains (1.94 Gm.) and more daily for at least two weeks, one patient taking from 30 to 60 grains (1.94 to 3.89 Gm.) daily for fourteen months, without any complaint. Unterberg [3b] also witnessed no mishaps in adults after doses of 15 grains (0.97 Gm.). Such reports support Vámossy and others who have expressed the belief that phenolphthalein is harmless to man. Besides these cases in which an overdose caused no ill effects, there are undoubtedly others, as such incidents are apt to pass unrecorded.

Influence of Age and Dosage on Frequency of General Reactions.—I have made a careful analysis of the case histories in the various reports listed in footnote 2. The reactions from phenolphthalein seemed to be entirely independent of the size of the dose and the age of the recipient. Certain of the general ill effects followed a single or occasional average dose of the drug. In nine instances the ill effects followed an overdose. A cumulative action may have caused a disturbance in six cases. The reactions were about equally divided between children and adults. To offset these there were at least eleven instances (six in children) in which no apparently unusual complaint ensued from an overdose.[12]

Symptoms and Pathogenesis of General Reactions.—The symptoms noted in such disturbances were, aside from purgation, not in the nature

10. (*a*) Brasch, G.: Phenolphthalein als Abführmittel nebst Bemerkungen über die Art der Einführung neuer Arzneimittel, Ztschr. f. Med.-Beamte **19**:450, 1906. (*b*) Gillette, H. F.: Accidental Overdose of Phenolphthalein, J. A. M. A. **51**:1782 (Nov. 21) 1908. (*c*) Kaminsky: Etude sur le purgène, Méd. mod. **15**:354, 1904. (*d*) Orland, F.: Ein Fall von unbeabsichtigter hoher Phenolpththaleindosis bei einem Kinde, Med. Klin. **9**:257, 1913. (*e*) Vámossy.[7] (*f*) Wenhardt.[5g]

11. Elmer, W. P.: The Action and Dosage of Phenolphthalein, M. Rec. **74**: 838, 1908.

12. Footnotes 10 and 11.

of a pharmacologic action of the drug. Whether produced by a small or by a large dose of phenolphthalein, they formed a varying syndrome in which circulatory, renal or nervous signs predominated.

Sollmann [13] referred to the reactions reported by Holz, Best, Zabel, Orland and others [14] and stated that "only a few doubtful cases are on record." It is possible that the unusual symptoms noted in some of the general reactions were not due to the drug but that some illness at the time either contributed to the general clinical picture or was entirely responsible for it. Recurrence of symptoms with repeated use of the drug is cited in only two cases.[15]

The doubt expressed regarding these general reactions is due to the inadequate data given in many of the reported cases, and also to the present lack of more exact knowledge of the action and properties of the drug. It is for that reason that certain reactions, among them two fatalities attributed to phenolphthalein,[16] are still considered as questionable in this study.

A poisonous action in the pharmacologic or toxicologic sense is apt to occur following an overdose of any drug, or when a drug is taken with sufficient frequency to produce cumulative effects. However, an overdose of phenolphthalein necessary to produce toxic symptoms is comparatively much higher than that of many other drugs. The absence of ill effects from an overdose in a number of cases indicates that a form of idiosyncrasy may exist in the persons who have a reaction from an overdose. The type of idiosyncrasy that exists when the reaction follows a single average dose is probably of a higher degree, pointing toward sensitization. Although in the published reports it was not stated that the patients had come in contact with the drug previously, some may have inadvertently done so and thus apparently become sensitized. Others may have had a family or personal history of atopy which accounted for their idiosyncrasy. Still others who took large doses without ill effects either were not hypersensitive or had become desensitized through continued use of the drug. The reason for making these assumptions in the case of the general reactions will perhaps be better understood when the cutaneous reactions have been considered.

REPORTS OF CUTANEOUS REACTIONS

In the discussion of the case of the first patient with an eruption due to phenolphthalein, presented by Howard Fox in 1917, doubt was expressed as to whether phenolphthalein could be the cause of

13. Sollmann, T.: A Manual of Pharmacology and Its Applications to Therapeutics and Toxicology, Philadelphia, W. B. Saunders Company, 1932, p. 237.

14. Footnotes 2 and 10*d*.

15. Lauze.[2n] Talley and Glenn.[2q]

16. Roux.[2l] Cleeves.[2s]

a cutaneous eruption.[17] The same patient came under my observation at the Vanderbilt Clinic and had a definite relapse when given a test dose of the drug.[18] The present resurvey [19] shows that other patients with cutaneous lesions characteristic of those produced by phenolphthalein apparently had been observed in this country as early as 1909 [20] and even earlier.[21]

The cases of definite eruption due to phenolphthalein reported number about one hundred and forty. The cutaneous lesions presented have been predominantly of the fixed erythematous type, and as they are well known they require no description here. Contrary to the reports of systemic disturbances, the cutaneous lesion can usually be corroborated by a flare-up of the old cutaneous lesions following the subsequent use of the drug.

Several factors were investigated to see if any could be demonstrated to be the cause of the cutaneous reactions. The factors bearing on the physicochemical nature of the drug itself will be discussed first; the others, dealing with the status of the affected person, will receive consideration later.

Yellow and White Varieties of Phenolphthalein.—Phenolphthalein is described in "The Pharmacopoeia of the United States of America" as a white or faintly yellowish-white crystalline powder. Before 1918 phenolphthalein was imported from Central Europe and was white. Since then white phenolphthalein and a yellow variety, which fulfils the requirements of the "Pharmacopoeia" except as to color, are almost entirely supplied by domestic concerns.

Without going into any great detail it may be stated that the main difference between the white and the yellow form of phenolphthalein is in the degree of purity. Phenolphthalein is prepared from two molecular parts of phenol and one of phthalic anhydride, with a condensing agent such as sulphuric acid or zinc chloride. On condensation the phenol components give up two hydrogen atoms to unite with one of oxygen freed from the phthalic anhydride. Phenolphthalein therefore

17. Fox, H.: Erythema Perstans Following Ingestion of Phenolphthalein, J. Cutan. Dis. **36**:252 (April) 1918. Presented before the Manhattan Dermatological Society April 13, 1917.

18. Abramowitz, E. W.: Erythema Multiforme Associated with Cutaneous Pigmentation (Melanin): Clinical and Pathologic Report of Five Cases, J. Cutan. Dis. **36**:11 (Jan.) 1918. (Received for publication April 5, 1917.)

19. (*a*) The first survey of various publications on dermatology for such cases prior to 1918 failed to reveal any so designated.[18] (*b*) See also Wise, F., and Abramowitz, E. W.: Phenolphthalein Eruptions, Arch. Dermat. & Syph. **5**:297 (March) 1922.

20. Trimble, W. B.: Purpura, J. Cutan. Dis. **27**:306, 1909.

21. Dr. E. Brockelmann of St. Louis in a recent personal communication informed me of three cases observed in 1905 but not reported.

contains three benzene rings in its structure, which is chemically p-p'-di-hydroxy-di-phenylphthalide ($C_{20}H_{14}O_4$). The white product is usually formed by repeated carbon decolorization of the cruder yellow variety. The greater the number of such decolorizations the whiter and also the more purified the drug. The purity of phenolphthalein may also be detected by differences in the melting point.

A few of the brands of yellow and white phenolphthalein which were examined revealed an excess in the yellow forms of a variable amount of a residue designated as "dark bodies." Small doses of the "dark bodies" produce purgation. Harmful impurities such as arsenic were not detected. Wood [9] and others noted the variation in doses of phenolphthalein required to produce a laxative effect in the same person. In the investigation reported here samples of phenolphthalein were tested in human subjects and also in monkeys (Macacus rhesus), and it was shown that the laxative dose of the white form is three times that of the yellow.[22] The form of phenolphthalein used in some of the preparations could therefore account for the variation in action that was sometimes noted. It had no influence, however, on the incidence of cutaneous eruptions in those who were susceptible. I have reproduced cutaneous eruptions by the use of either yellow or white phenolphthalein in the same person. A similar observation was reported by Novy.[23] There is no apparent reason for the belief held by some that the white variety of the drug does not cause a cutaneous eruption.

In the reports cited in footnote 2 the general reactions noted up to 1918 were presumably from the white variety of phenolphthalein obtained from Central Europe. Similar reactions were also reported later that were due to the presence in some preparations of the yellow form of phenolphthalein. Therefore, the form of the drug has no bearing on the incidence of the general ill effects.

In view of the smaller dose of yellow phenolphthalein required to produce a laxative action, it is not surprising that this form is being used in some preparations rather than the white phenolphthalein, U. S. P. Purification of the drug seems to lessen its effectiveness and raises the question of the necessary presence of excess "dark bodies" for superior therapeutic results. Some brands of the yellow variety are slightly more active than others, perhaps owing to differences in the proportion of this residue.

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22. Williams, E. F., Jr.; Abramowitz, E. W., and Killian, J. A.: The Value of the Monkey for the Study of the Laxative Activity of Phenolphthalein, Especially in Comparing Different Samples of the Drug, J. Lab. & Clin. Med. **19**:1213 (Aug.) 1934.

23. Novy, F. G.: Phenolphthalein Eruption; Experimental Data on Its Causation, Arch. Dermat. & Syph. **26**:125 (July) 1932.

Effect of Ingredients, Various Derivatives and Aromatic (Benzene Ring) Compounds Related to Phenolphthalein: Conjugated Phenolphthalein.—Soon after the ingestion of phenolphthalein about 90 per cent of the drug is found as free phenolphthalein in the stool and occasionally in minute quantities in the urine. Ordinarily no trace of the drug can be found in the excretions after about four days. Traces of the drug are found in the blood of animals after intravenous injections of the substance. Apparently no demonstrable quantity of phenol is set free in the system of the person who takes phenolphthalein. I have had these findings corroborated. Occasionally in this investigation small traces of phthalic acid could be detected in the urine. Kastle,[24] after intraperitoneal injections of phenolphthalein into a guinea-pig, observed the presence of conjugated phenolphthalein in the urine. Abel and Rowntree [25] noted it in the bile of dogs after subcutaneous injections of the drug. In one half of the normal subjects studied I found that the conjugate appeared in the urine in small quantities eight hours after the ingestion of the drug and could no longer be detected after twenty-four hours. One patient with a recent fixed eruption due to phenolphthalein showed no trace of the conjugate in the urine.

Novy [23] administered various derivatives of phenolphthalein and related compounds to a patient subject to phenolphthalein eruptions, and there was no recurrence of the eruption. I administered to a similar patient and to a control the following substances, each showing one or several benzene rings in its chemical structure, and none caused any evident flare-up in the previously affected areas of the skin:

Phenol: one drop in milk by mouth, three times daily for two days; no reaction.

Phthalic anhydride: one dose of 485 mg. by mouth; no reaction.

Phthalic acid: one dose of 300 mg. by mouth; no reaction.

B-mono-hydroxy anthraquinone: one dose of 0.03 Gm. by mouth; no reaction.

Alizarin (1-2 di-hydroxy anthraquinone): 150 mg. by mouth; no reaction.

Quinizarin (1-4 di-hydroxy anthraquinone): 150 mg. by mouth; no reaction.

Chrysazin (1-8 di-hydroxy anthraquinone, a laxative sold under the name of "Istizin" and from which eruptions resembling those due to phenolphthalein are reported): 0.3 Gm. by mouth; no reaction.

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24. Kastle, J. H.: The Conduct of Phenolphthalein in the Animal Organism, U. S. Pub. Health Serv., Hygienic Laboratory, bull. 26, 1906, p. 23.

25. Abel, J. J., and Rowntree, L. G.: On the Pharmacological Action of Some Phthaleins and Their Derivatives, with Especial Reference to Their Behavior as Purgatives, J. Pharmacol. & Exper. Therap. **1**:231 (June 8) 1909-1910.

Di - hydroxy-di - phenyl - isatin and di - acetyl-di - oxyphenyl - isatin (Isacen) (two of the newer laxatives somewhat like phenolphthalein in action): 1 dose of 5 mg. by mouth; no reaction.

Tyrosine (b-hydroxy-phenyl-alanine) and dopa (I-di-oxyphenyl-alanine): 93 mg. by mouth; no reaction. Tyrosine and dopa were used because of their relation to the formation of pigment, which is often noted as a sequel of rashes due to phenolphthalein.

Tetra-iodophenolphthalein sodium was not administered as it occasionally produces eruptions, and this was not desired at the time in this patient. It was given (1 Gm.) to another patient with an eruption due to phenolphthalein, but no reaction was produced at the site of the old lesions.

Phenol tetra-chlor-phthalein: 25 mg. by mouth; no reaction.

Phenolsulphonphthalein: 6 mg. intravenously; no reaction.

These tests with negative results may be interpreted as excluding phenol and phthalic anhydride (which are used in the preparation of phenolphthalein) and the other aromatic compounds related to phenolphthalein as a cause of the eruptions due to this laxative.

The presence of "dark bodies" had been noted by others in various forms of phenolphthalein, especially the yellow variety. These "dark bodies" are acid but of an undetermined chemical structure, and have hitherto never been entirely freed of traces of phenolphthalein, which clings to them tenaciously. A barium salt of the "dark bodies" which was free from phenolphthalein was finally prepared by Edward F. Williams Jr., and 1 mg. of this substance was given to a patient who had been shown to be affected with a rash due to phenolphthalein. A mild laxative action occurred about a day later, but there was no flare-up in the patient's old lesion. This test was repeated on the same patient with 2 mg. doses with similar results.

The question of the presence in the skin of phenolphthalein, especially in the early stage of an eruption due to phenolphthalein, has thus far been answered in the negative. In three definite instances chemical analysis of an excised lesion (erythematous type) showed that none of the drug was present. In view of the fact that phenolphthalein can be detected in a dilution as high as 1:12,000,000, this seems at first sight to be final. Sulzberger [26] examined the contents of a bullous lesion produced by phenolphthalein but found no trace of the drug. I could not find free phenolphthalein or the conjugate in a similar case. However, further investigation for the presence of phenolphthalein and also of the conjugate compound, particularly in those patients who have bullous eruptions, is necessary since chemical analysis for anti-

26. Sulzberger, M. B.: Personal communication.

pyrine in fixed bullous lesions produced by that drug has revealed that the drug is present in the fluid contents of the bullae.[27]

Effect of the Vehicle in Which Phenolphthalein Is Administered.—Phenolphthalein can be obtained as a powder, capsule or tablet. It is used as a household remedy mainly in the form of a chocolate or gum confection. It is incorporated in oily emulsions and is also used with various products, such as bile salts, other cathartics, and agar, psyllium seeds, etc. My studies have shown that the laxative action of phenolphthalein is somewhat enhanced when the drug is ingested in an alcoholic solution. Loewe [28] showed that the use of a colloidal suspension of the drug, presumably the white variety, in an emulsified liquid petrolatum reduced the required dose of phenolphthalein and also decreased its toxic action. These results were questioned by Kaufman,[29] particularly as the experiments by Loewe were carried out on mice and not on human beings. This has been one of the major difficulties in the past with investigations of phenolphthalein. The drug was usually found to be inactive in all animals hitherto tested, except when administered in relatively huge doses, usually requiring repetition. My studies, however, have definitely established that in monkeys (Macacus rhesus) the usual laxative effects are obtained following doses comparable to those that are effective in the human subject.[22]

It may be of interest to note that there are reports of eleven instances in which typical cutaneous eruptions were produced by preparations of the drug in liquid petrolatum. In the report of one of these cases it was stated that no ill effects followed the use of the laxative in a chocolate confection.[30]

Idiosyncrasy.—The cutaneous eruptions produced by phenolphthalein, except in four instances, followed the usual dose. Symptoms of a general nature often accompanied these reactions and ocasionally were pronounced. The cases of cutaneous reactions in which the systemic symptoms were dominant were classed as of the general type. The history obtained in some of the cases in which eruptions developed indicated that the patient had taken phenolphthalein on occasions for several months or longer without any apparent ill effects. Corson and Sidlick [31] mentioned a case in which the eruption appeared suddenly

27. (*a*) Tonnel and Raviart: Erythèmes bulleux dus à l'ingestion d'antipyrine; leur pathogénie, Echo méd. du nord **1**:18, 1897. (*b*) Mibelli, V.: Ueber die fixen Antipyrinerytheme, Monatschr. f. prakt. Dermat. **26**:533, 1898.

28. Loewe, S., and Lange, F.: Entgiftetes Phenolphthalein, Klin. Wchnschr. **9**:207 (Feb. 2) 1930.

29. Kaufman, E.: Entgiftetes Phenolphthalein, Klin. Wchnschr. **10**:1219, 1931.

30. Fox, H.: Phenolphthalein Eruption with Bullae, Arch. Dermat. & Syph. **26**:741 (Oct.) 1932.

31. Corson, E. F., and Sidlick, D. M.: Urticaria from Habitual Use of Phenolphthalein, J. A. M. A. **78**:882 (March 25) 1922.

after the remedy had been employed for two years without any mishap. The idiosyncrasy shown by these persons to the drug can hardly be attributed to a cumulative action, since the interval between the stated doses is known to be much longer than the ordinary period (four days) which is required for the excretion of the drug. The idiosyncrasy to this drug was apparently acquired, therefore, in certain cases through a sudden inexplicable development of hypersensitivity. Traces of phenolphthalein could be found in the stool until the ninth day in one case of phenolphthalein eruption in which there was also albuminuria of long standing. This has thus far proved to be an exceptional case.

The eruption may occasionally be of familial occurrence. Stancanelli [32] and Virga [33] each reported cutaneous lesions from phenolphthalein in a mother and two children. Virga expressed the belief that the sensitization developed in utero because the mother took the drug during pregnancy. He said that the exanthem developed the first time the drug was taken. There are still other cases in which the cutaneous eruption apparently appeared following the first dose of the drug. It is difficult to state the exact proportion of patients who react to the first dose and those who react only after repeated doses, mainly because such information is based on the patient's statement. It is conceivable, however, that those who react to the first dose have inadvertently come in contact with phenolphthalein previously, since this drug is occasionally found in such unsuspected substances as cookies and dentrifices.

Newman [2u] noted a recurrence of the cutaneous lesions after a patient had received a dose of ½ grain (0.03 Gm.) of phenolphthalein. I reported [34] the case of a young woman who had had several severe previous outbreaks due to phenolphthalein in whom a mild relapse occurred six years later after she ate iced cup cakes containing an unknown but infinitesimal amount of phenolphthalein. Other drugs, such as acetylsalicylic acid, amidopyrine, quinine, etc., had been well tolerated during that time. The small amounts of phenolphthalein capable of causing a relapse of the cutaneous lesions indicate hypersensitiveness, and the fact that this drug alone and none of the others mentioned caused the eruption demonstrates that the hypersensitivity was specific. This specificity was also evident in the absence of reactions in my experimental subject when related chemical compounds were administered. Group hypersensitiveness is, however, possible, as is

32. Stancanelli, P.: Dermatitie eritemato-pemfigoide recidivante de origine medicamentosa (fenolftaleina), Dermosifilografo **3**:10 (Jan.) 1928.

33. Virga, E.: Erythèmes pigmentés fixes par phénolphtaléine, Dermosifilografo **3**:675 (July) 1932.

34. Abramowitz, E. W.: Phenolphthalein Eruption Produced by the Eating of Iced Cup Cakes, M. J. & Rec. **136**:31 (July 6) 1932.

shown by a case reported by Cannon [35] in which the subject was also intolerant to acetylsalicylic acid.

My first publication dealing with the eruptions produced by phenolphthalein [18] was not labeled as such as only one (case 5) of the five patients studied had a recurrence after an experimental dose of the drug. The others [36] with similar eruptions showed no evident flare-up of old lesions. Thus a state of temporary desensitization, a "refractory period" or "negative phase," sometimes developed. An instance of apparent desensitization of long standing was observed in one case, in which a cutaneous reaction following an overdose failed to recur when the use of the drug was resumed after a lapse of ten years.[37]

Patch tests with phenolphthalein (yellow and white) in alcoholic solution and oily suspension were reported to be negative by Wise and Sulzberger [38] in patients subject to the fixed eruptions due to phenolphthalein. The results were negative both on the normal and on the previously affected areas of the skin. Bernstein [39] succeeded in obtaining a positive reaction to a patch test with a relapse of an eczematous type of eruption due to phenolphthalein. Wise and Sulzberger in their publication reported a similar result in a patient with an eczematous eruption of the hands (dermatophytid?). They have recently encountered another patient with eczematous lesions on the chest who had been taking "Agarol" and who gave positive reactions to patch tests with both white and yellow phenolphthalein but not with the "dark body" component of the drug and controls.[40] There are occasional reports of positive patch [41] and intracutaneous tests [42] in patients with the fixed type of phenolphthalein eruptions, but these tests are usually negative. My own studies have shown negative patch tests with phenolphthalein, numerous derivatives of phenolphthalein and other compounds previously listed. Intradermal tests were abandoned as unreliable because of the insolubility of the drug and the irritating nature of some of the solvents (alcohol, alkalis and oils). The negative skin tests reported

35. Cannon, A. B.: Dermatitis Medicamentosa (Phenolphthalein), Arch. Dermat. & Syph. **24**:899 (Nov.) 1931.

36. One patient (footnote 18, case 4) had a recurrence ten years later after taking a sugar-coated gum laxative containing phenolphthalein.

37. Personal observation.

38. Wise, F., and Sulzberger, M. B.: Drug Eruptions, Arch. Dermat. & Syph. **27**:549 (April) 1933.

39. Bernstein, F.: Ueberempfindlichkeit gegen Phenolphthalein, Dermat. Ztschr. **62**:368 (Dec.) 1931.

40. Wise, F., and Sulzberger, M. B.: Personal communication.

41. Joltrain, in discussion on Milian and Mourrut: Erythème fixe récidivant dû aux laxatifs à base de phénolphtaléine, Bull. Soc. franç. de dermat. et syph. **39**:1672 (Dec.) 1932.

42. Brockelmann.[29] Cannon.[35]

in most of the cases of fixed phenolphthalein eruptions are somewhat offset by the positive results in the cases of more recently recognized eczematous lesions produced by this drug.

Bloch [43] reported that some observers had been able to obtain a passive transfer in cutaneous reactions due to such drugs as neoarsphenamine, antipyrine and mercury. Kobayashi [44] was successful in obtaining a passive transfer in the case of a fixed eruption due to phenolphthalein.[45] The reagins, or antibodies, while regularly present in diseases due to hypersensitivity, such as asthma, hay fever, generalized neurodermatitis and some forms of urticaria, prurigo and infantile eczema, are not found as a rule in cases of hypersensitiveness due to drugs or other agents.

It is shown that while phenolphthalein in the ordinary dosage is inherently nontoxic for normal persons, minute amounts of the substance can produce a recurrence of symptoms in a patient previously brought in contact with the offending agent and such reactions are specific for that particular substance. On the other hand some persons showing hypersensitivity may become desensitized, while still others are not hypersensitive and can tolerate large doses from the beginning. The symptoms of the reactions attributed to hypersensitivity are entirely different from those due to a pharmacologic action. Cumulative effects in many cases of eruptions due to phenolphthalein are apparently eliminated. These observations speak for the close relationship of the idiosyncrasy to phenolphthalein with other known allergic sensitizations, such as sensitization to other drugs and to plants, foods, foreign proteins and bacterial products.

Naegeli and his co-workers [46] by means of a Thiersch graft succeeded in transplanting the hypersensitiveness in a fixed eruption due to antipyrine to a previously unaffected area of the skin of the same patient. Urbach,[47] after repeating this experiment with analogous results in a patient with an eruption due to phenolphthalein, was inclined to believe that such fixed lesions demonstrated local hypersensitiveness that originated in the epidermis. Wise and Sulzberger [38] also performed

43. Bloch, Bruno: The Rôle of Idiosyncrasy and Allergy in Dermatology, Arch. Dermat. & Syph. **19**:192 (Feb.) 1929.

44. Kobayashi, Utaka: Ein Fall von Laxatol-Exanthem, Jap. J. Dermat. & Urol. **31**:86, 1931.

45. Another investigator using a modification of the Walzer method has recently reported a successful passive transfer (Kenedy, D.: Sulla ipersensibilita, Gior. ital. di dermat. e sif. **75**:965 [April] 1934).

46. Naegeli, de Quervain and Stalder: Nachweis des zellulären Sitzes der Allergie beim fixen Antipyrinexanthem (Autotransplantationen, Versuch in Vitro), Klin. Wchnschr. **9**:924 (May 17) 1930.

47. Urbach, E., and Sidaravičius, B.: Zur Kritik der Methoden der passiven Uebertragung der Ueberempfindlichkeit, Klin. Wchnschr. **9**:2095 (Nov. 8) 1930.

an autotransplant with a fixed type of lesion due to phenolphthalein, but they used a full thickness skin graft. A recurrence took place not at the site of the transplanted area but where the fixed eruption had been. A similar observation was recorded by Loveman,[48] who used a technic similar to that of Naegeli, in a fixed eruption from alurate. According to Wise and Sulzberger, the result of their experiments, confirmed by Loveman, suggests that the forces governing the sensitization of the transplant probably originate below the thickness of the graft, perhaps in the neurovascular network supplying the area that is the seat of the eruption. This view receives additional support from the histologic observations in the cases of fixed eruptions due to antipyrine and to phenolphthalein. The inflammatory effects in such cases are perivascular and predominantly in the cutis.[49] Further experiments of this kind are, however, needed to locate definitely the site in the skin where this hypersensitiveness originates. As the general symptoms show that other tissues at times are the seat of the reaction, it may be that the same mode of pathogenesis applies to them also.

In view of the many basic similarities between the idiosyncrasy to phenolphthalein and the manifestations of hypersensitiveness due to specific sensitization, there is apparently a form of specific allergic hypersensitiveness in persons who have eruptions due to phenolphthalein. It is plausible to assume that other tissues besides the skin may become sensitized similarly, accounting for the general reactions which are not due to an overdose or to cumulative effects. As a certain number of persons can tolerate large doses of phenolphthalein, reactions in others from an overdose may be due not to the toxic action alone but possibly in part to sensitization or some other contributing cause.

SUMMARY AND CONCLUSIONS

A survey of the entire literature on reactions to phenolphthalein shows that the reports deal mainly with the general constitutional effects (various syndromes in which circulatory, renal or nervous disturbances predominate) and with cutaneous eruptions. Certain of the general reactions need to be verified. The cutaneous eruptions are characteristic. The total number of reactions observed is small if one considers the extensive use of the drug.

Most of the cutaneous reactions and certain of the general effects were noted after the use of a single or occasional average dose of the drug. The number of systemic disturbances resulting from an overdose (nine cases) and the possible instances of cumulative action (six cases)

48. Loveman, A. B.: Experimental Aspect of Fixed Eruption Due to Alurate, a Compound of Allonal, J. A. M. A. **102**:97 (Jan. 13) 1934.

49. Abramowitz.[18] Mibelli.[27b]

are somewhat offset by at least eleven reported instances of no apparent ill effects from an overdose. The age of the recipient could also be excluded as a factor of any importance as the reactions occurred almost equally in children and adults.

White phenolphthalein, U. S. P., and yellow varieties are being used in various preparations. The yellow phenolphthalein is a less highly refined product and contains more of a residue known as the "dark bodies," which apparently possesses purgative properties. The laxative dose of the white variety is three times that of the yellow. Either form of the drug is capable of producing reactions.

Other physicochemical factors, such as phenol and phthalic anhydride (from which phenolphthalein is prepared), various derivatives and aromatic (benzene ring) compounds related to phenolphthalein, could not be found to be responsible, after ingestion or by skin tests, for the cutaneous lesions. The vehicle in which the drug was administered had no apparent effect on the incidence of the eruptions. Phenolphthalein or its conjugate compound could not be demonstrated in the fixed eruptions produced by the drug.

Chemical and microscopic examination of the blood and urine, including blood counts, in normal persons before and after the use of the drug showed that no noticeable changes took place.

While phenolphthalein in the ordinary dosage is inherently nontoxic in normal persons, small doses may produce a recurrence of symptoms (fixed eruptions) in a person who has once been so affected.

Eruptions due to phenolphthalein may appear after the first dose, suggesting that there has been previous contact with the drug in unsuspected substances, such as certain dentrifices and cookies, or sensitization in utero, if the mother took the drug while pregnant. In other instances the occasional use of an average dose may bring on the sudden development of hypersensitivity.

Phenolphthalein, but none of the other commoner drugs, reproduced the cutaneous lesions. Phenolphthalein thus simulates the action of a specific excitant in persons who have been previously sensitized. In a few instances a person with an eruption due to phenolphthalein became desensitized, as no recurrence of the cutaneous lesions occurred when he resumed the use of the drug. Those who took large doses without any ill effects at any time apparently were not hypersensitive.

These observations and the dissimilarity between the pharmocologic action and the symptoms noted in those persons showing an idiosyncrasy to phenolphthalein speak for the close relationship of this idiosyncrasy with other known allergic sensitizations such as sensitization to other drugs and to plants, foods, foreign proteins and bacterial products.

The conventional skin tests are usually negative in cases in which there are eruptions due to phenolphthalein, with the exception of the

few reported cases of eczematous lesions. Reagins (antibodies), while regularly present in cases of disease due to hypersensitivity, such as asthma, hay fever, generalized neurodermatitis and some forms of urticaria, prurigo and infantile eczema, are not found as a rule in cases of hypersensitiveness to a drug or some other agent.

Experiments with autotransplant skin grafts seem to demonstrate that fixed eruptions due to antipyrine, phenolphthalein and alurate represent local areas of cutaneous hypersensitiveness, which can be reproduced at will by the specific excitant.

In view of the many basic similarities between the idiosyncrasy to phenolphthalein and the manifestations of hypersensitiveness due to specific sensitization, there is apparently a form of specific hypersensitiveness, allergic in nature, in the patients who have eruptions due to phenolphthalein. It is plausible to assume that other tissues besides the skin may become sensitized similarly, thus accounting for the general reactions that develop which are not due to an overdose or to cumulative effects. As a certain number of persons can tolerate large doses of phenolphthalein, reactions in other persons following an overdose may be due not to the toxic action alone but possibly in part to sensitization or to some other contributing cause.

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ABSTRACT OF DISCUSSION

DR. RICHARD S. WEISS, St. Louis: This paper is highly interesting and instructive. There has been an increasing number of these cases.

One patient, whom I saw in the City Hospital a few years ago, was covered with bullous lesions which were surrounded by a halo of pigmentation. For three months the lesions recurred on the skin and were not accompanied with any generalized reaction or symptom except slight fever at times. There was no leukocytosis or any other change in the blood. At first the condition was thought to be pemphigus or an extreme case of bullous erythema multiforme, but it was finally discovered that the patient's wife was bringing him a preparation which contained phenolphthalein and which was proved to be the cause of the eruption. When the eruption faded, the pigmented areas remained. The patient continued to take phenolphthalein at intervals, and when he entered the Barnard Free Skin and Cancer Hospital in 1932 his skin was covered with dark gray pigmentation which varied in intensity in different areas. The pigmentation has faded little since 1932. Argyria could be definitely ruled out. The dopa reaction demonstrated in the sections an apparent increase in the dendritic cells. The silver nitrate stain showed a marked increase in the deposit of pigment in the basal layer of the epidermis. (This case will be reported in full in a later issue of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.)

DR. ISADORE ROSEN, New York: I wish to emphasize one point in particular regarding this interesting paper of Dr. Abramowitz, namely, that when an eruption is suspected to be due to a drug it is highly important in testing the patient's susceptibility to give only a small dose. The case of a patient who was recently under my observation illustrates the danger attached to testing the idiosyncrasy. A man, aged 63, came to the clinic because of a generalized eruption, which I

suspected was due to phenolphthalein. From the history it was found that he had not taken any drugs during the past two and a half years but that the eruption had persisted during that time. He was given 1 grain (0.065 Gm.) of phenolphthalein with directions to take it when he reached home. One hour after taking the tablet he became unconscious and had convulsive seizures and the sphincters were paralyzed. His family called in an ambulance surgeon who used every measure to revive him. After four hours the patient regained consciousness and for four or five days was confined to his bed. When I saw the patient seventy-two hours after he had taken the drug, the original purplish-blue areas of pigmentation were markedly aggravated, the face and neck were swollen and the entire body below the axillae was diffusely bluish red and edematous. The eruption could then be recognized as typical of that produced by phenolphthalein. It is possible that the severity of the symptoms was due to the physical state of the patient, as he had marked myocarditis, endocarditis and extensive vascular disease.

Dr. Hamilton Montgomery, Rochester, Minn.: I wish to emphasize what Dr. Rosen has said about using large amounts of phenolphthalein for testing. Some years ago I gave a laborer 5 grains (0.324 Gm.) of phenolphthalein in order to be sure to demonstrate the reaction for students the following day. The patient had a severe reaction with a temperature of 104 F., which necessitated hospitalization for several days.

Dr. Earl D. Osborne, Buffalo: I wish to obtain some information. A patient of mine who had a typical eruption due to phenolphthalein had taken the drug in the form of "liver pills" for seven years. The eruption was almost generalized one year ago. Since then the patient has stopped taking the drug and the lesions have gradually decreased in severity and in size, but she still has some lesions. In consulting the literature from a pharmacologic standpoint, it appears that phenolphthalein is toxic to the liver and in some cases has produced a definite hepatitis with enlargement of the liver and presumably a storing of the drug in the hepatic tissue. In view of the fact that Dr. Abramowitz stated that phenolphthalein is rapidly eliminated through the kidneys and bowels within a short time, it seems that this question of storage of phenolphthalein in the liver is of great importance following the long continued ingestion of the drug. Does Dr. Abramowitz have any data as to the length of time for which the drug can be stored in the liver?

Dr. Fred Wise, New York: It is evident that phenolphthalein is not a poison but rather a sensitizing agent, such as a pollen or a dye. As Dr. Abramowitz pointed out, one patient may have a severe reaction from a minute dose, while another may suffer no ill effects from an enormous dose.

It has been demonstrated that the drug acts on the vascular structures of the skin and that the corium is the point of attack. However, a patient is occasionally observed in whom an eczematous reaction attacks the epidermis and in whom patch tests should exhibit positive results.

In one patient (Mr. L., previously reported) to whom 1 grain (0.065 Gm.) of yellow phenolphthalein was administered, a reaction appeared within two minutes after the tablet was swallowed. His face suddenly became red and began to itch, and the areas of eruption on the body, which had almost faded, flared up and began to itch intensely. He complained of dizziness and malaise a few minutes after swallowing the drug. In another patient (Miss K.) a faded eruption due to phenolphthalein flared up in situ after she had taken no drug other than a barbital derivative with amidopyrine for three months.

Dr. C. Guy Lane, Boston: In regard to test doses, I have two cases in mind. In one instance the patient had had an eruption similar to that due to

phenolphthalein but had none at the time. She was instructed to take ½ grain (0.032 Gm.) of phenolphthalein, but through a mistake of the nurse she was given 1 grain (0.065 Gm.). Within a short time her temperature rose, a typical eruption developed and morphine was required for two nights.

Another case was that of a man who knew he was sensitive to phenolphthalein; he had been warned about it and had kept away from any laxative medicament except saline preparations. An eruption developed following a test dose, and on close questioning it was found that he had bought some cup cakes and eaten them. He had an extremely severe eruption not only in the areas that had previously flared up and were still pigmented but over the whole body, and he was extremely uncomfortable for two or three days.

Dr. Karl G. Zwick, Cincinnati: There are on the market several qualities of phenolphthalein which seem to differ from each other not only in appearance and color but also in therapeutic activity. I am led to consider this last possibility because I find that the container of one of the proprietary preparations bears the statement that the product contains phenolphthalein "specially prepared, not U. S. Pharmacopoeia." From such a claim one might conclude that the various kinds of phenolphthalein may also differ from each other not only in their desirable therapeutic properties but also in their eczematogenic qualities or that a chemically definable contamination or impurity may be the causative materies peccans in the development of cutaneous symptoms. In view of these circumstances I am prompted to ask Dr. Abramowitz whether his investigations give any information in regard to the points mentioned.

It may be of interest to relate how the laxative action of phenolphthalein was accidentally discovered a long time after it had been used by the chemists as an indicator in the titration of acids and alkalis. The discovery came about through the recommendation made by a chemist to the Hungarian government to add a trace of phenolphthalein to the Tokay wine intended for home consumption. Subsequently, the addition was made at the time the state tax was paid, and if any wine on sale in Hungary was found to contain no phenolphthalein (i. e., if the wine in question failed to turn red with alkalis), that was considered evidence that the state had been defrauded. Bibulous persons, especially tourists not inured to the *vin du pays,* were liable to have diarrhea. I recall that for some time the phenolphthalein tablets sold in Europe came from Budapest. An American manufacturer of a proprietary preparation employed phenolphthalein to differentiate his product and to detect imitations.

Dr. E. William Abramowitz, New York: I am glad to have Dr. Weiss confirm by means of the dopa reaction that the pigmentation in eruptions due to phenolphthalein is caused by melanin. In this paper I have attempted to demonstrate that reactions following the usual dose of phenolphthalein are the result of an idiosyncrasy produced by sensitization. The cases cited by Dr. Rosen and Dr. Montgomery seem to support this assumption. Dr. Lane's observation that an eruption may follow the ingestion of minute amounts of phenolphthalein in the icing of cup cakes is interesting. It is perhaps in this and other ways that some patients unknowingly become sensitized to the drug, and what is presumably a reaction after the first dose is actually a reaction due to sensitization brought about by previous contact with phenolphthalein. It is advisable that only small doses of phenolphthalein (½ grain [0.032 Gm.] or less) should be used in testing patients suspected of having an eruption due to phenolphthalein. The same applies to cases of susceptibility to other drugs. Some of the proprietary preparations contain yellow phenolphthalein. The U. S. P. preparation dispensed by the druggist is

the white form of the drug, but I wish to emphasize again that reactions may be produced from either the white or the yellow phenolphthalein. In answer to Dr. Osborne's question as to whether or not phenolphthalein is toxic to the liver, I may state that while the literature shows that the halogen salts of phenolphthalein can cause necrosis of the liver, no instance has been reported of any hepatotoxic effects due to phenolphthalein itself. Phenolphthalein seemed to be effective in cases of catarrhal jaundice in children and adults, the drug still acting as a purgative in spite of the absence of bile. (Suzor: Progrès méd. **17**:463, 1903. Tunnicliffe, F. W.: Brit. M. J. **2**:1224 [Oct. 18] 1902). Wood believed that this drug was more or less of a cholagogue (Philadelphia General Hosp. Rep. **7**:183, 1909). I agree with Dr. Wise that phenolphthalein cannot be classed as a poison in view of the numerous instances reported in which an overdose has passed off without any alarming symptoms. Further knowledge of the action and properties of the drug is necessary before it will be possible to interpret correctly some of the reported general reactions attributed to phenolphthalein.

Answering Dr. Zwick as to the presence of any other poisonous ingredients in phenolphthalein, I may say that analyses of several brands show that there are no traces of arsenic. The yellow phenolphthaleins are more active because they seem to contain more of the "dark bodies." There is also some variation between the various white and yellow forms of the drug, owing to the differences in the method of manufacture.

ADDENDA

Since this article was submitted for publication the following additional references have been noted:

Sachs (Accidental Overdose of Phenolphthalein in a Child Without Ill Effects, J. A. M. A. **104**:45 [Jan. 5] 1935) reported the case of a child, 3½ years old, who ingested 96 grains (6.2 Gm.) of yellow phenolphthalein with no ill effects, excepting some purgative action and a single mild attack of vomiting. This is the largest overdose of phenolphthalein reported in the literature.

Fantus, in a personal communication, stated that the variation in action sometimes noted in the same person from the same brand of phenolphthalein may also depend on the hydrogen ion concentration of the contents of the colon. This may be the reason why phenolphthalein must be taken in larger doses by some persons.

Ota and Sato (Fixe Laxatolexanthem, die durch Mileval verschlimmerten, Jap. J. Dermat. & Urol. **36**:83 [Oct.] 1934) reported that laxatol (acetyl isovalerianate of phenolphthalein) caused a fixed cutaneous eruption to appear. This eruption later recurred in the same patient when he took mileval (Isacen [di-acetyl-di-oxyphenyl-isatin]).

In reference to the successful passive transfer reported by Kenedy,[45] Sulzberger and I repeated this experiment on ourselves and on two others as controls. We were unable to confirm Kenedy's findings. Careful interpretation of such experiments are necessary as normal serums occasionally give false positive readings.

A STUDY OF CRUDE COAL TAR AND ALLIED SUBSTANCES

PRELIMINARY REPORT

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AND

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In dealing with the problem of tar one must first define what is meant by tar. To use the term "tar" as if it were a definite chemical compound, readily obtainable from the pharmacist, is erroneous. A brief résumé of the present, somewhat limited, knowledge of tars in general will illustrate this. Much of the information has been gathered from the writings of Porter [1] and Perutz and Siebert.[2] Since the latter authors have covered all the older literature on the subject we shall not cite it here. A few of the more recent publications have been cited by Nelson and Osterberg.[3]

Any product obtained by destructive distillation of organic substances is a tar. It is thus readily understood that the chemical composition of tars varies with the substances from which they were derived and with the temperatures to which they are subjected. There are four main groups of organic material from which therapeutically used tars can be obtained, namely, wood, coal, bitumen and crude petroleum.

WOOD TARS

The wood tars comprise: Oleum cadini (juniper); oleum fagi (beech); oleum rusci (birch); pix pini (pine); pix navalis, the residue of wood tar distillation—of interest only because it was used for epila-

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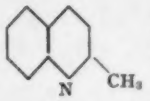
* This work was instituted during tenure of fellowship under the Douglas Smith Foundation for Medical Research.

1. Porter, H. C.: Coal Carbonization, New York, The Chemical Catalog Co., Inc., 1924.

2. Perutz, A., and Siebert, C.: Pharmakologie der Haut: Arzneimittel, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 5, pt. 1.

3. Nelson, Marque O., and Osterberg, Arnold E.: A Purified Coal-Tar Ointment for the Treatment of Infantile Eczema, Arch. Dermat. & Syph. **15**:669 (June) 1927.

tion as emplastrum picis navalis—cadogel, a distillate of oleum cadini (a light brown, almost odorless liquid), and pittylen, a product of condensation of oleum rusci and formaldehyde.

The difference in the chemical composition of wood and coal tars lies mainly in the absence in the wood tars of certain substances of a basic character, such as pyridine , quinoline and quinaldine (alpha-methyl quinoline ). Furthermore, the wood tars do not have a photosensitizing effect (Fleischhauer [4]).

COAL TARS

The coal tars comprise the following pharmaceutic preparations:

Pix lithranthracis (oleum lithranthracis), ordinary crude coal tar.

Extractum lithranthracis, the ether-soluble and benzol-soluble portion of coal tar, a synonym of which is liquor anthracis simplex (Fischel).

Liantral, a coal tar from which the free particles of carbon have been removed—a thick, black liquid which contains all the substances having a boiling point of about 80 C. (176 F.).

Lithantrol (K. Herxheimer), a coal tar combined with chlor-ethyl alcoholate.

Carboneol (K. Herxheimer), obtained by dissolving coal tar in carbon tetrachloride and the residue in chloroform.

Numerous attempts have been made to eliminate the most obvious practical obstacle in tar therapy—the black color. The methods used to achieve decolorization differ. One method is as follows: One part of liquor carbonis detergens (coal tar solution, N. F.) and two parts of tincture of quillaja or tincture of hippocastanum (horse-chestnut) are macerated for eight days, and the mixture is filtered. The filtrate is a brown liquid which can be decolorized by precipitation with lead acetate—liquor carbonis detergens decoloratus.

The principle in this process is the attempted fixation of certain constituents of coal tar to the saponin (probably a glycoside) which is present in various vegetable tinctures. The preparations include:

Tar alba, a fraction of coal tar removed from the crude product by distillation with steam (Nelson and Osterberg [3]).

Supertah a proprietary ointment similar in appearance to tar alba.

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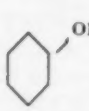
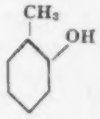
4. Fleischhauer, L.: Sensitization of Skin to Light by Means of Liantral, Strahlentherapie **36**:144, 1930.

The "active principle fraction of crude coal tar," a distillate which comes off between the temperatures of 170 and 300 C., from which the naphthalene is removed (Jaffrey [5]).

Anthrasol, a mixture of equal parts of "purified" coal tar and juniper wood tar.

Sulfanthren, a proprietary ointment containing purified coal tar and sulphur.

All these more or less colorless substances seem to have one property in common—their total pharmacologic effect is usually less than that of the original crude coal tar. This is by no means surprising if one studies the chemical properties of coal tar and considers the wide range of possibilities of chemical changes during the process of manufacture.

Crude coal tar is characterized by the predominating occurrence of aromatic hydrocarbons, such as benzol , toluol , naphthalene and anthracene . Of the phenolic constituents one finds phenol  , cresol  and various polyhydroxyphenols. Coal tar shows an alkaline reaction in contrast to the wood tars, which have an acid reaction. As already mentioned, this reaction is due to the content of basic substances. Chemical analyses show that almost 48 per cent of the ordinary coal tar is composed of hydrocarbons (of which 32 per cent are of an unknown structure), 42 per cent of carbon and asphalt and 10 per cent of water.

By dry distillation the following substances are obtained:

70 to 160 C.: the light oils (benzol, toluol, xylene and pyridine).

150 to 220 C: the medium oils (naphtha, heavy benzene, crude phenol and cresols).

220 to 260 C.: the heavy oils (naphthalene, creosols, quinoline and other liquid and solid hydrocarbons).

260 to 400 C.: the anthracene oils (fluorescent green oil, containing as one of the constituents acridine and some of its derivatives, such as carbolineum).

The remainder consists of pitch (carbon and asphalt).

5. Jaffrey, W. R.: A Report on the Therapeutically Active Principle Fraction of Crude Coal Tar, Canad. M. A. J. **18**:680, 1928.

CHEMISTRY OF TARS

The chemical composition of coal tar naturally varies with the origin of the material (the type of coal) and with the temperature at which the tar was produced. The quantity also influences the product—the smaller the retort, the more uniform are the batches of tar. Tar distilled at a high temperature differs in important aspects, such as physical characteristics and chemical composition, from tar distilled at a low temperature. High temperature tar is a black, rather thick, viscous liquid, much heavier than water; it is made up chiefly of hydrocarbons, of which the solid aromatic compounds form a large proportion, mixed with a high percentage of free carbon, from 3 to 7 per cent of phenolic compounds, and small quantities of liquid aromatics, nitrogenous bases and compounds of sulphur. Paraffin hydrocarbons and unsaturated compounds are, in the main, absent. On the other hand, low temperature tar is a relatively thin liquid, only slightly heavier than water, which contains no solid aromatics, almost no free carbon, a predominating quantity of hydrogenated ring compounds with paraffin side chains and a large percentage (varying from 10 to 40) of complex high-boiling phenolic compounds. Unsaturated compounds are also present in fairly large amounts. This fact cannot be overemphasized, since there is reason to suspect that the easily oxidized substances represent the active constituents of crude coal tar (experimental work).

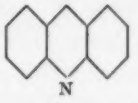
The essential difference in chemical composition between high and low temperature tars is baffling only if one does not realize that the complex compounds of tar are actually produced during the process of distillation. None of the constituents of coal tar probably exists as such in the coal. Tar is not, in a true sense, distilled from coal. It results, more properly speaking, from condensation of the liquid products of the decomposition of coal by heat. In this step-by-step decomposition, the chemical structure of the products depends on the temperature employed. The decomposition which takes place at high temperatures, for example, considerably affects the phenols and napthalenes, which are the principal sources of the monocyclic and polycyclic aromatic hydrocarbons, respectively. At high temperatures, also, a larger amount of free carbon is formed, which renders the tar heavy and thick and the content of pitch high.

It is thus apparent that for dermatologic purposes only low temperature tar should be used.

A tar which with respect to the uniformity of composition is ideal for use in experimentation is the "Bergin" tar, the product of hydrogenation of coal by the Bergius process. However, in spite of being

therapeutically active,[6] this product differs considerably from ordinary coal tar in that it contains many hydrogenated substances which during the ordinary process of tar production are split into carbon or coke.

A complete pharmacologic evaluation of coal tar has not yet been carried out. It is generally assumed that the antipruritic effect of coal tar is due to the phenols and cresols. However, in addition to its antipruritic effect, coal tar has definite antiacanthotic, vasoconstrictive, keratoplastic and antiparasitic effects. It is by virtue of the first three properties enumerated that crude coal tar is made use of in the treatment of psoriasis.

Which particular substance or group of substances is responsible for the therapeutic effect? This question is not easily answered. Information has been gathered concerning the injurious effect of some of the substances contained in crude coal tar. Thus naphthalene, it is claimed, is an irritant, and so are the phenols and cresols in a higher concentration. Among the heavy oils, fluorescent green oil is the most interesting because it contains acridine (di-benzo-pyridine) 

. Acridine has a photodynamic effect, and it is suggestive that the combined effect of ultraviolet radiation and coal tar in the treatment of psoriasis may be due to that substance.

The photosensitizing effect of coal tar has been studied by us, as well as by Goeckerman,[7] Herrick and Sheard,[8] Daubresse-Morelle,[9] Allison,[10] Kuznitsky and Jacoby[11] and Fleischhauer.[4] Herrick and Sheard showed that a photochemical change occurs when coal tar is exposed to ultraviolet radiation. They think it possible that, by this means, a new compound is formed which is responsible for the beneficial effect. New light on this problem was shed by Fleischhauer.[4] It

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6. Rottman, H. G.: Coal Tar Therapy with Liquid Carbon (Bergin), Dermat. Wchnschr. **84**:534 (April 16) 1927.

7. Goeckerman, W. H.: Treatment of Psoriasis, Northwest Med. **24**:229 (May) 1929; Treatment of Psoriasis: Continued Observations on Use of Crude Coal Tar and Ultraviolet Light, Arch. Dermat. & Syph. **24**:446 (Sept.) 1931.

8. Herrick, J., and Sheard, C.: Effects of Irradiation of Crude Coal Tar by Quartz Mercury Vapor Lamps: I. Evidence of Chemical Changes as Shown by Changes in Absorption Spectra, Proc. Soc. Exper. Biol. & Med. **26**:33 (Oct.) 1928.

9. Daubresse-Morelle, E.: L'actinothérapie générale associée aux applications de goudron dans le traitement du psoriasis, J. belge radiol. **18**:336, 1929.

10. Allison, J. R.: Tar and Quartz Light Therapy, South. M. J. **22**:592 (June) 1929.

11. Kuznitsky, E., and Jacoby, H.: Sensitivity of X-Ray Skin and Tar Skin to X-Rays, Ultraviolet Light Rays and Alpha Rays, Arch. f. Dermat. u. Syph. **156**:136, 1928.

was shown, first, that only the coal tars are photosensitizing, while the wood tars, cresols, phenols, naphthols and chrysarobin are not, and, second, that the presence of the coal tar preparation during irradiation is unnecessary. The reaction to radiation is even stronger when the coal tar has been completely removed from the skin prior to irradiation; the reaction can be demonstrated even if coal tar is applied to the skin for as short a period as fifteen minutes and if the skin is irradiated as late as seventy-two hours after complete removal of the tar. Third, the reaction is not brought about only by irradiation with a quartz lamp, but to an even more marked degree by exposure to sunlight shining through an ordinary glass window. Thus it seems that temporary sensitization of the epidermis is effected by applications of even short duration and that this sensitization is directed toward rays which include the short wave rays of visible light and the long wave ultraviolet rays. This observation is of special interest since Urbach and Konrad [12] showed that photosensitization-induced dermatosis of the type of prurigo aestivalis (Hutchinson) is likewise caused by visible rays which range on the borderline between red and yellow.

Bloch and Widmar [13] worked on the carcinogenic effect of coal tar. It was found that carcinoma is produced in mice by the fraction obtained at a temperature of from 230 to 300 C. The active fraction is soluble in benzol. The authors failed to isolate a single active chemical compound responsible for the production of cancer, and they expressed the belief that the carcinogenic substances are probably anthracene oils, which contain no nitrogen, sulphur or arsenic. Recently, however, the isolation of the carcinogenic substance in British shale was successfully accomplished by Cook and his co-workers.[14] It was found to be the hydrocarbon 1 : 2 benz-pyrene:

Perutz,[2] in the summary of his chapter on tar, stated: "The analysis of the effect of tar shows that the light and medium oils do not have

12. Urbach, E., and Konrad, J.: Ueber eine durch den langwelligen Anteil des Sonnenspektrums erzeugte Lichtdermatose vom Typus der Prurigo aestivalis Hutchinson: Die lichtschützende Wirkung des Resorcin, Strahlentherapie **32**:193, 1929.

13. Bloch, Bruno, and Widmar, F. E.: Weitere Untersuchungen über die bei der künstlichen Krebserzeugung wirksamen Teerbestandteile, Arch. f. Dermat. u. Syph. **152**:529, 1926.

14. Cook, J. W.; Hewett, C. L., and Hieger, I.: The Isolation of a Cancer-Producing Hydrocarbon from Coal Tar, J. Chem. Soc. **1**:395, 1933.

a specific effect; yet they are important in that they control resorption and thereby prevent an excessive effect. The heavy oils and pitch are responsible for the keratoplastic effect. The points of attack are the basal cell and prickle cell layers. The sphere of action of tar extends to the connective tissue and the vascular system. It may produce phenomena ranging from a keratoplastic effect to the production of blastoma."

BITUMINOUS TARS

The bituminous tars comprise the following pharmaceutic preparations:

Ichthyol ammonium sulpho-ichthyolicum.

Ichthulene, a product similar to ichthyol (International Bitumen Co., Bitumont, Alberta, Canada).

Sodium sulpho-ichthyolicum
Calcium sulpho-ichthyolicum
Ichthalbin (ichthyol albuminate)
} for internal use.

Ichthoform, a condensation product of formaldehyde and ichthyo-di-sulphuric acid.

Ichtoxyl (Samberger), a mixture of pulverized ichthyol and another substance which splits off oxygen when brought in contact with living tissue.

Bitumol.

Thigenol.

Tumenol (ammonium tumenolicum and oleum tumenoli).

Thiol siccum and thiol liquidum.

Eutirsol (decolorized bituminous oil).

If "bituminous formations" are distilled the tars obtained are called bituminous oils. The "tar" obtained from "bituminous formations" containing the fossil remains of fish is called "raw ichthyol." Bituminous tars differ from coal and wood tars in that they contain a considerable amount of sulphur. In raw ichthyol, for example, about 10 per cent of sulphur is present in the form of compounds of thiophen $\left[\begin{matrix} CH=CH \\ | \\ CH=CH \end{matrix}\!>\!S\right]$. The sulphur content of coal tar is negligible (2:1,000).

The pharmacologic effect of this group of tars is not based alone on the presence of derivatives of thiophen because thiophen itself is inert. It seems that special conditions are necessary to develop a bituminous oil which gives the effect of sulphonated bitumen. According

to Potonié [15] and Scheibler,[16] the oil must originate in part, at least, from animal remains, but only if formed under nonoxidizing conditions will it be effective. Furthermore, it must be unsaturated (as evidenced by the "heating up" reaction with sulphuric acid). On saturation of the unsaturated compounds its therapeutic effect is reduced to that of a mild preparation of sulphur.

The method of producing sulphonated bitumen is briefly as follows: The raw bituminous oil, of which as much as about 50 per cent consists of thiophen compounds, the rest being composed of hydrocarbons and nitrogenous compounds, is treated with sulphuric acid to form ichthyosulphuric acid. This is warmed with a saturated solution of sodium chloride to remove free sulphuric acid and sulphur dioxide. Free ichthyosulphuric acid, which is insoluble in a saturated solution of sodium chloride, is precipitated; it is then washed, neutralized with ammonia and evaporated until it has reached the consistency of syrup. The product is ammonium sulpho-ichthyolicum or sulphonated bitumen. Its chief component (from 55 to 56 per cent) is a dry substance consisting of the ammonium salts of sulphonic acids derived from the thiophen compounds of the raw oil. Its sulphur content is about 11 per cent.

PETROLEUM TARS

Another class of tars, of less practical importance, are those derived from the distillation of crude petroleum. The petroleum tars comprise the following pharmaceutic preparations: naphtalan (obtained by the distillation of Armenian petroleum) and nafalan (same as naphtalan).

Experimental work on distillation of tar derived from crude petroleum was performed by Shibata.[17] He merely found that its action is noncarcinogenic.

EXPERIMENTAL STUDY

In a study of crude coal tar and allied substances it seemed logical to choose as a standard for comparison a condition of the skin in which the therapeutic value of tar is generally accepted. This seems to be the case with psoriasis; its treatment by the combined use of crude coal tar and ultraviolet radiation, as inaugurated by Goeckerman,[7] has stood the test of time and is in general use in many of the institutions of this

15. Potonié, Robert: Neues zur Erdölentstehung, Naturwissenschaften **20**:279 (April) 1932; Das Muttergestein des Ichthyols, Pharm. Ztg. **78**:908 (Sept.) 1933.

16. Scheibler, Helmuth: Ueber die chemischen Bestandteile der schwefelreichen, bituminösen Teeröle (Ichthyolöle), Ber. d. deutsch. chem. Gesellsch. **48**:1815, 1915; **49**:2535, 1916; **52**:1903, 1919.

17. Shibata, S.: Experimental Study of Tar: Action of Tar Obtained from Crude Petroleum by Distillation, Acta dermat. **14**:94 (July) 1929.

country. Since Goeckerman's preliminary work several publications on the subject have followed.[18]

The object of our study was twofold: (1) to obtain a better knowledge of the pharmacologic action of crude coal tar and (2) to obtain a product which would retain the therapeutic qualities of tar and at the same time render the treatment of psoriasis a cleaner procedure, so that it could be carried out conveniently at home.

An idea of the complexity of the first problem may be obtained from what has already been said. How can a more definite knowledge of the action of the various components of coal tar be obtained? Three methods of approach to this study readily suggest themselves. Short exploratory attempts were made to determine the most suitable way of attacking the problem.[19]

I. *Fractional Distillation in High Vacuum.*—By this method various fractions are obtained. It should be possible to evaluate the therapeutic action of each fraction. The most active fraction might then be further fractionated into several subfractions, each of which in turn might be tested therapeutically. It should thus be possible, at least theoretically, to isolate an active substance or a group of active substances responsible for the effect.

It should be mentioned in this connection that attempts to isolate the therapeutically active fraction from coal tar by fractional distillation (not including the studies which were made on the carcinogenic effect of tars) were made by Nelson and Osterberg [3] and Jaffrey [5] and by practically all the commercial concerns which supply the medical profession with proprietary preparations of tar.

This method of evaluation, while theoretically sound, has numerous practical drawbacks in that it is impossible to evaluate quantitatively the different fractions.

The fractional distillations in high vacuum were carried out as follows: [20]

A measured amount of ordinary crude coal tar (distilled at 800 F. and uniform in the different batches), obtained from the gas-works of Urbana, Ill., was placed in a flask to which a glass tube leading to a condenser was sealed. From the first condenser a glass tube led to a second condenser and from this to an oil pump reenforced by a mercury vapor pump. The second condenser was cooled by means of carbon

18. Daubresse-Morelle.[9] Allison.[10]

19. Dr. M. S. Kharasch, Professor of Chemistry at the University of Chicago, assisted in this work.

20. Dr. M. Adeline Bloodgood of the Department of Chemistry, University of Chicago, carried out part of the distillations.

dioxide snow. The system was evacuated to a pressure of 2 mm. The following observations were made:

As the distillation was carried out it was noted that at about 85 C. under a pressure of 2 mm., a light yellow liquid was distilled. As the temperature rose to 125 C. yellow crystals were noticed. They were collected in a receiver. With a further rise in temperature the color of the distillate changed from yellow to light brown. Most of the distillate was collected at a temperature below 300 C.; above that temperature little material came over. An asphalt-like mass remained in the distilling flask. The color of the distillate, while light when first obtained, changed in time to dark, particularly when exposed to air.

Ordinarily three fractions were collected—one at about 150 C., one at about 270 C. and the third at the high boiling point of the substance.

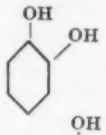
II. *Separation by Solvents.*—The separation was attempted by shaking crude coal tar with di-butyl ether. Two portions were obtained: (*a*) The ether-soluble portion, which, after the ether has been removed by distillation, is a black liquid of low specific gravity.

(*b*) The nonsoluble portion, an almost crystalline, nongummy, light brown material, mixed with carbon.

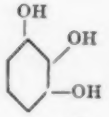
III. *Use of Specific Chemicals.*—The shortcomings of the first and second methods and certain observations made during the experiments caused us to wonder whether it might not be possible to reach our objective by substituting certain chemical compounds for crude coal tar and evaluating them clinically. We examined the classes of substances in successful use today in the treatment of psoriasis, and we were struck by the fact that most of them, while chemically distinct, possess a common property—they are all strong reducing agents (chrysarobin, anthralin). It appeared reasonable to assume that the active constituents of crude coal tar also belong chemically to the same group. The presence of a reducing agent and of easily oxidized substances in crude coal tar is indicated by the fact that when freshly distilled tar is light in color but when exposed to the air it assumes at once a dark color. The extent of the darkening is directly proportional to the time of exposure. This definitely suggests, therefore, the presence in crude coal tar of very strong reducing substances, for the number of substances which combine directly with the oxygen of the air is limited to the most powerful reducing substances, such as tri-hydroxy-benzene, the various types of aminophenols, hydroxy-quinoline, etc. Besides these reducing substances there are nonreducing compounds present in crude coal tar, all of which, so far as is known, have been tried therapeutically with no success (anthracene, naphthalene, etc.). It appeared reasonable,

therefore, that an attempt at investigation along the line indicated should include tests on substances of the following structures:

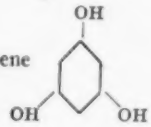
Catechol or ortho-dihydroxy-benzene



Pyrogallol or 1, 2, 3, tri-hydroxy-benzene

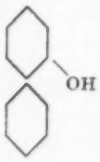


Phloroglucinol or 1, 3, 5 tri-hydroxy-benzene

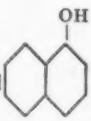


Para-amino phenol

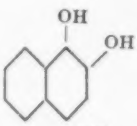
Hydroxy-di-phenol



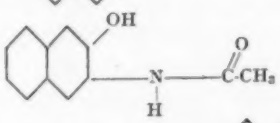
Alpha-naphthol and beta-naphthol



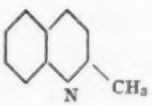
Hydroxy-naphthol



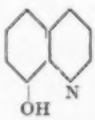
Naphtanil-A S



Quinaldine or alpha-methyl-quinoline



8-hydroxy-quinoline



The clinical evaluation of our experimental work was done exclusively on hospitalized patients with psoriasis for the reasons stated at the beginning of the paper. Each patient was subjected to the regular

treatment, which consisted of: a diet restricted in proteins; a daily colloidal bath; biweekly autohemic injections for five weeks; daily generalized ultraviolet irradiation in ascending suberythema doses, and local applications of a 5 per cent crude coal tar ointment, prepared according to the formula of White.[21]

In certain (usually corresponding) areas substances obtained by experimental work were substituted for the ordinary crude coal tar ointment. In most cases these substances were used in the same concentration and worked up in the same base as ordinary crude coal tar. However, sometimes we used the substances in higher concentrations or in the pure form in order to determine the absence or presence of irritating effects. In order to study the influence of ultraviolet light only one half of the body was irradiated in most cases.

The results obtained with the various substances were as follows:

I. *Products of Distillation* (Thirteen Cases).—For practical purposes we shall refer to the products of distillation as the low, middle and high fractions and pitch, designating by the first terms the three fractions collected at various temperatures, as mentioned in the experimental part, and by the latter term the nondistillable residue of the distilling flask.

1. Low Fraction: This product was found to be definitely inferior to crude coal tar in about one half of the cases, while in the other half the patients responded equally well to the two substances. In about one half of the patients an irritating effect was observed, and this result was obtained in spite of the low concentration of the fraction (2.5 per cent) as compared with that of crude coal tar (5 per cent). Lesions irradiated with ultraviolet light responded better than the lesions to which no ultraviolet radiation was given.

2. Middle Fraction: This product was found to be definitely inferior to crude coal tar in about the same proportion of cases as the low fraction. It did not check parakeratosis as well as did crude coal tar, since scaling of the lesions was prolonged. An irritating effect was present in a few cases, but this was less common than with the low fraction. The combined effect of ultraviolet irradiation and the middle fraction was less pronounced but was still present.

3. High Fraction: The results were indefinite. However, it is our opinion that the high fraction seems to be more effective than the low and middle fractions. It was found to be the least irritating of the three products. The favorable influence of ultraviolet irradiation was noted.

4. Pitch: The results were indefinite, but the action was irritating.

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21. White, Charles J.: Poisoning by Crude Coal Tar, J. Cutan. Dis. **34**:497 (July) 1916; Crude Coal Tar in Dermatology, Arch. Dermat. & Syph. **4**:796 (Dec.) 1921.

II. *Solvent-Separated Substances* (Five Cases).—Both the ether-soluble and the nonsoluble portion had about the same therapeutic effect as crude coal tar. Folliculitis, which is a common complication when crude coal tar is used for a certain length of time, occurred with the ether-soluble, but not with the nonsoluble, portion. In a case of extremely stubborn pustular psoriasis, marked erythema developed on the exposed side of the body as a result of ultraviolet irradiation. The erythema progressed to diffuse psoriasis. In spite of this complication, the irradiated side showed a far better response to treatment than the nonirradiated side in the areas treated by both portions and by crude coal tar.

III. *Specific Chemicals* (Nine Cases).—Of all the substances which were tried none was equal to crude coal tar. Catechol and 8-hydroxy-quinoline, had a decided effect. No sensitizing effect with ultraviolet radiation was noted. Pyrogallol and lenigallol were only slightly inferior to crude coal tar, but the former substance caused irritation. Catechol absorbed the infiltrate as rapidly as crude coal tar, but erythema and slight scaling remained after a period in which crude coal tar had cleared the lesions completely. 8-hydroxy-quinoline was irritating in some cases. Beta-naphthol seemed to act well in checking the spread of parakeratosis, but it failed later to bring the lesions to absorption.

RESULTS

Before drawing conclusions we wish to emphasize that any statement must be taken *cum grano salis,* for the reason that exact observation of therapeutic effects in cases of psoriasis entails great difficulties even when the patients are hospitalized. It is well known that general measures are sometimes sufficient to clear up a psoriatic eruption. In a number of cases we observed that areas used as controls (either left entirely untreated or treated with petrolatum only) cleared at about the same rate. This occurred particularly in the cases in which no difference could be found in the therapeutic value of the different materials. We believe, therefore, that the results in these cases should be evaluated with the greatest caution, and hence we shall draw our conclusions not on the basis of the percentage in all the patients treated, but on the percentage in only about one-half the patients, those in whom the response to treatment in general was slow and the individual therapeutic effect on each area treated was therefore more distinct.

Experiments with the distilled fractions showed that each fraction had a therapeutic effect, but to a less marked degree than the whole tar. The high temperature fraction seemed to have the best effect. Likewise, the effect of each fraction was enhanced by ultraviolet irradiation. The irritating quality of tar seems to be due to substances

which decrease in amount with an increase in the temperature at which the fraction was removed.

The results obtained with the solvent-separated products seemed to show that the therapeutic and, likewise, the photosensitizing effect are present in both portions. Substances which are responsible for development of folliculitis from the application of tar are contained in the ether-soluble portion.

The results of the experiments with the action of specific chemicals seem to indicate that certain reducing chemical substances of the type of catechol and 8-hydroxy-quinoline justify a more extensive study, particularly in view of the fact that the first two methods of approach to the problem of tar fail to clarify the situation. Thus, high fractional distillation in vacuum does not separate the fractions quantitatively, thus rendering distinct evaluation impossible. Neither does the method of separation by solvents bring about a separation of the portions from the active and nonactive principles of crude coal tar. We believe, therefore, that the method of approach by the action of specific chemicals offers the greatest promise.

There is another series of compounds which has not yet been taken into consideration. We wish to mention in this connection that we have found a group of chemical substances to be of value which seem to work on an altogether different basis, namely, by the stimulation of tissues. This, however, will be the subject of a separate report.

BITUMEN

In conclusion, the bituminous tars will be briefly discussed. Because of their name we thought it advisable to compare their effects with those of crude coal tar. One would expect that, as both substances are essentially tars, their pharmacologic effects would be somewhat similar, or that bituminous tar would show the effect of tar plus that of sulphur, owing to the abundance of sulphur compounds. This is not the case. We investigated the therapeutic value of sulphonated bitumen, ichthulene and a bituminous oil which is obtained in Utah. Ichthulene was found to have therapeutic properties similar to those of sulphonated bitumen. These substances failed to show the therapeutic qualities of crude coal tar. Their effect was not enhanced by ultraviolet irradiation. An attempt to induce such an effect by adding 1 per cent of eosin to the bitumen ointment was unsuccessful.

An investigation was also made of a domestic product of the group of petroleum tars ("Mid-Continent Residue," derived from the distillation of Oklahoma and Texas crude oil at from 700 to 800 F.), representing 25 per cent per volume of the original crude oil (Standard Oil Company). It did not show a tarlike effect, and if its use was

followed by irradiation, erythema was not produced. It proved to be nonirritating to the skin.

SUMMARY

The chemistry and pharmacologic action of the various tars are presented briefly.

Studies made on psoriatic patients revealed that:

1. Distillates of crude coal tar have a tarlike effect, but to a less marked degree than that produced by the whole tar. High temperature fractions seem to have the best effect. The effect of each fraction is enhanced by ultraviolet irradiation. The irritating quality of crude coal tar is due to substances contained in the lower fractions.

2. If crude coal tar is separated by solvents (di-buthyl ether), both portions have a therapeutic effect which is increased by photo-irradiation. Folliculitis results from the application of the ether-soluble portion only.

3. Owing to shortcomings in the first two methods, a method of approach by the use of specific chemicals was adopted. It seems to reveal that certain reducing chemical substances such as catechol, 8-hydroxy-quinoline are promising with respect to their tarlike pharmacologic effect. We are now studying the comparative effects of the reduced and the oxidized forms of this compound.

4. Sulphonated bituminous tars do not have the therapeutic qualities of crude coal tar. They are not photosensitizers. American sulphonated bitumen is equal in effect to the sulphonated bitumen from Europe.

5. Petroleum tar has neither a tarlike nor a photosensitizing effect.

THE ARSENIC PROBLEM

REPORT OF A CASE OF PROBABLE ARSENIC DERMATITIS FROM WEARING APPAREL

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Several decades ago arsenic was alleged to be a normal constituent of the body,[1] but that claim has been much disputed. In recent times through the investigations of Throne and Myers [2] and their co-workers and others [3] renewed interest has been aroused in the occurrence of

1. Gautier, A.: Sur l'existence normale de l'arsenic chez les animaux et la localization dans certains organes, Compt. rend. Acad. d. sc. **129**:929, 1899.

2. (*a*) Fordyce, J. A.; Rosen, I., and Myers, C. N.: Quantitative Studies in Syphilis from a Clinical and Biologic Point of View; Normal Arsenic, Arch. Int. Med. **31**:739 (May) 1923. (*b*) Myers, C. N., and Cornwall, L. H.: Normal Arsenic and Its Significance from the Point of View of Legal Medicine, Am. J. Syph. **9**:647 (Oct.) 1925. (*c*) Throne, B., and Myers, C. N.: New York State J. Med. **26**:843, 1926. (*d*) Myers, C. N.; Van Dyck, L., and Throne, B.: Arsenic as a Problem in Present Day Public Health Management, M. Times **57**:134, 1929. (*e*) Throne, B.; Van Dyck, L. S.; Marples, E., and Myers, C. N.: Arsenic Findings in Dermatologic Conditions, New York State J. Med. **27**:757, 1927. (*f*) Myers, C. N., and Throne, B.: The Relation of Arsenic to Public Health, ibid. **29**:871, 1929. (*g*) Van Dyck, L.; Throne, B., and Myers, C. N.: Arsenic Findings in Eczema and Allied Conditions in Infants and Young Children, Arch. Pediat. **47**:218 (April) 1930. (*h*) Myers, C. N.; Throne, B., and Kingsbury, J. J.: Toxic Action of Metals in Alopecia Areata, New York State J. Med. **33**:991, 1933.

3. (*a*) Vogel, K.: The Significance of Arsenic in the Excretions, Am. J. M. Sc. **176**:215 (Aug.) 1928. (*b*) Kraetzer, A. F.: Raynaud's Disease Associated with Chronic Arsenical Retention, J. A. M. A. **94**:1035 (April 5) 1930. (*c*) Shelden, N. D.; Doyle, J. B., and Osterberg, A. E.: Neuritis from Arsenic and Lead, Arch. Neurol. & Psychiat. **27**:322 (Feb.) 1932. (*d*) O'Leary, P. A.; Snell, A. M., and Bannack, E. G.: Portal Cirrhosis Associated with Chronic Inorganic Arsenical Poisoning, J. A. M. A. **90**:1856 (June 9) 1928. (*e*) Distribution of Arsenicals in the Body, editorial, ibid. **91**:805 (Sept. 15) 1928. (*f*) Oliver, T.: Elimination of Arsenic After Sheep-Dipping, Lancet **2**:740 (Oct. 4) 1930. (*g*) Lowenburg, H., and Naide, M.: Arsenic Poisoning Caused by a Mouth Wash Containing a Solution of Potassium Arsenite, J. A. M. A. **100**:737 (March 11) 1933. (*h*) Stoddart, W. O.; Riddell, A. R., and Bulmer, R. M. R.: Arsenic as a Potential Hazard for the Farmer, Canad. M. A. J. **27**:264 (Sept.) 1932. (*i*) Halloran, C.: Dermatitis Exfoliative Due to Arsenic in Wall Paper, Arch. Dermat. & Syph. **20**:303 (Sept.) 1929. (*j*) Thorel and Vinzent: A propros d'une intoxication collective par l'arsenic, Ann. de dermat. et de syph. **3**:618, 1932. (*k*) Willcox, W. N.: Acute Arsenical Poisoning, Brit. M. J. **2**:118 (July 22) 1922. (*l*) The Occurrence of Arsenic in the Body, editorial, J. A. M. A. **81**:478 (Aug. 11) 1923. (*m*) Ayres, S., Jr., and Anderson, N. P.: Cutaneous Mani-

(Footnote continued on next page)

arsenic in the tissues and excretions of the body both in health and in disease. This work has emphasized the widespread use of arsenic and the countless possibilities for its absorption into the body. Water, dust, soil, food, drugs and articles of wearing apparel and of household use apparently are all potential sources of arsenic poisoning. Fordyce, Rosen and Myers [2a] showed that arsenic is found "normally" in a large number of persons, depending on the character of their food, drink, medication and environment. Later, as a result of tests made on a large series of normal persons, Myers and Cornwall [2b] concluded that 0.4 mg. of arsenic per hundred grams of dried specimen is the normal value for urine (according to Howard [4] the presence of arsenic in the urine does not indicate an abnormal condition unless the amount exceeds $\frac{1}{200}$ grain per gallon, or 0.0075 mg. per hundred cubic centimeters), that 0.3 mg. per hundred grams of dried specimen is the normal value for the blood and that arsenic is a normal constituent of the hair. As a result of their examination Myers and Cornwall concluded from a conservative point of view that arsenic is undoubtedly a customary constituent of the body and that it is derived from the ingestion of food or medication.

The enormous amount of research that has been devoted to the problem of arsenic poisoning has brought to the fore the question as to what significance can be attached to the presence of arsenic in the excretions of a patient who shows symptoms that might justly be attributed to arsenic poisoning even though the amount excreted is within "normal limits." The more intensely one studies the literature on this subject the more one becomes aware of the impossibility of drawing conclusions in specific cases.

The following case demonstrates this difficulty and emphasizes a somewhat neglected source of arsenic poisoning.

REPORT OF A CASE

A. F., a woman aged 23 years, was first seen on Feb. 10, 1934. In March 1933 an itching eruption developed on the anterior portion of the neck and gradually spread to the sides of the neck, face, shoulders and upper parts of the arms. The

festations of Arsenic Poisoning, Arch. Dermat. & Syph. **30**:35 (July) 1934. (*n*) Osborne, E. D.: Microchemical Studies of Arsenic in Arsenical Pigmentation and Keratoses, ibid. **12**:773 (Dec.) 1925; Microchemical Studies of Arsenic in Arsenical Dermatitis, ibid. **18**:37 (July) 1928. (*o*) Brooks, H. G., and Roberts, Leslie: The Action of Arsenic on the Skin as Observed in Recent Epidemic of Arsenical Beer Poisoning, Brit. J. Dermat. **13**:121, 1901. (*p*) Evans, W. V.: Arsenic Poisoning from Sprayed Asparagus, J. A. M. A. **99**:2202 (Dec. 24) 1932. (*q*) Food Poisoning Reported [Arsenic in Fresh Mustard Greens], Medical News, ibid. **97**:1971 (Dec. 26) 1931.

4. Howard, Tasker: Arsenic Poisoning, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1924, vol. 8, p. 86.

eruption continued until the summer of 1933, when it slowly disappeared. With the advent of cold weather, the eruption reappeared with gradual extension and acute exacerbations. There was no history of internal medication.

Examination revealed an extensive, acutely erythematous, scaling and crusted eruption with numerous excoriations involving the scalp, face, neck, back, upper extremities and chest. On the forearms were many discrete, keratotic papules, the size of a pinhead and larger, suggesting those seen in Darier's disease. There were tender, palpable enlargements of the glands on both sides of the neck. In the folds of the skin on the elbows, in the axillae and on the neck there was distinct fissuring. Otherwise physical examination revealed no abnormalities. The blood count showed: hemoglobin, 79 per cent; leukocytes, 11,400, and erythrocytes, 4,200,000. The differential count was: polymorphonuclear neutrophils, 78 per cent; lymphocytes, 20 per cent; transitional cells, 1 per cent, and undifferentiated cells, 1 per cent. The urine contained arsenic, but a quantitative test was not made.

At the Columbia Hospital the patient was given colloid baths; soothing ointments and lotions were applied, and calcium was given internally. The dermatitis responded to this treatment readily. The patient was questioned in an effort to associate the dermatitis with some external irritant. She said that prior to the onset of the dermatitis in 1933 she had begun to wear a new black woollen suit. During the summer of 1933 she did not wear the suit, and the dermatitis disappeared, but in the fall when she again wore the suit, the dermatitis reappeared.

Contact tests which were made with the suit material, rouge, several face creams, powder, a fur coat and a hair tonic all gave negative results. Because of the presence of arsenic in the urine, an analysis of the material of the suit was made. The hospital chemist reported that the dye found in the material was not fast even in physiologic solution of sodium chloride. The washings from the cloth contained small amounts of arsenic which must have been readily available when the skin was damp with perspiration.

Another sample of cloth from the suit was analyzed through the courtesy of Mr. J. Shuder, chemist of the E. I. Du Pont De Nemours Company. He reported: "There is 0.1 per cent arsenic in the 'analine black' which was used in dyeing the garment. Arsenic acid is used only as an oxidizing agent. The practice was stopped several years ago at our plant, and sodium chlorate is now used. When arsenic acid is used, it can and should be removed by a purifying process and the dye should then be analyzed to determine the arsenic content."

A third sample of the cloth was sent to another laboratory which reported a content of 0.013 mg. of arsenic for each gram of material.

After the patient's hair was washed tests showed that it contained arsenic. A hair tonic had not been used for several weeks before the test was made, and the hair had been washed frequently.

In a communication received about six weeks after her dismissal from the hospital, the patient stated that the dermatitis had healed but that there still was some residual pruritus.

COMMENT

Dermatologists and clinicians are confronted frequently with such problems as generalized dermatitis, peripheral neuritis, hepatitis or other manifestations, of sudden or slow onset, in conjunction with the presence of arsenic in the hair and in the excretions (urine and stools) without a definite history of exposure to arsenic than by chance every-day contacts.

The frequency with which arsenic occurs in the body in healthy persons is probably not well known. Arsenic may gain entrance to the body from food, water or other beverages,[5] clothes, articles that one handles and perhaps even the air that one breathes. The present widespread use of arsenic as an insecticide probably is the source of the most common means by which this chemical gains entrance into the body, namely, from food, for fruits and vegetables may carry the residue of an arsenical spray. For this reason food in order to be eligible for acceptance by the Committee on Foods of the American Medical Association cannot contain in excess of 1.06 parts of arsenic per million parts of food, or 1.4 parts of arsenic as arsenic trioxide per million parts of food. These tolerances have been established by the United States Department of Agriculture.[6]

Because of the frequency with which it has been found in the human body and in its excretions, especially urine, arsenic has come to be regarded as a "normal" finding. As arsenic is not known to be a necessary constituent of normally functioning tissues, it is questionable whether its presence in the body or in the urine is normal. It may rather represent a deposit from outside sources which may or may not cause disease. An arsenic deposit is commonly found in fact, it is usually noted, but nevertheless it is not a normal finding.[3b]

When confronted by a patient whose symptoms might be attributed to arsenic poisoning and in whose excretions arsenic is present, with or without a known source, what conclusions can be drawn? Is one justified in assuming that elimination of arsenic in any amount is of clinical significance, especially if symptoms exist that may be consistently attributed to the element? Sheldon, Doyle and Osterberg [3c] stated that the amount of arsenic eliminated furnishes no reliable guide to the physical injury that is, or may be, wrought by it, since it is the retained arsenic that does the harm. A general rule regarding the behavior of arsenic within the body is of little value because in many persons the biochemical reactions are exceptional. The intolerance or hypersensitiveness to arsenic shown by certain persons is well exemplified by the reactions to arsphenamine which are commonly seen. Certainly, those who suffer from symptoms of arsenic poisoning are exceptions. Little is gained, therefore, by knowing that in a large series of apparently normal persons 0.4 mg. per hundred grams of dried specimen is the average amount of arsenic found in the urine or that arsenic is a "normal" constituent of hair, because, as stated earlier, arsenic cannot be considered to be a "normal" constituent of the tissues or organs of

5. Thorel and Vinzent. [3j] Brooks and Roberts.[30]

6. Tolerance for Arsenic, Copper and Leads in Foods, report of the Committee on Foods, J. A. M. A. **101**:1483 (Nov. 4) 1933.

the body and, moreover, it is not the amount of arsenic eliminated but the amount retained that does the harm. This leads to the logical assumption that in cases of arsenic poisoning there is a specific reaction, or hypersensitiveness, of the affected person to arsenic. If not, then the element must be considered of no consequence, because the presence of arsenic in normal persons does not produce symptoms.[2c]

DIFFICULTIES IN EVALUATING THE RÔLE OF ARSENIC

In attempting to identify arsenic as a cause of disease, Kraetzer [3b] stated that the following postulates must be strictly observed:

1. There must be a definite history of unequivocal exposure. The mere chance that contamination has been produced by outside sources is not sufficient.

2. Arsenic must be quantitatively demonstrated in the urine.

3. Cure must follow the administration of sodium thiosulphate. Before the final establishment of cure, progressive improvement should parallel the course of treatment.

4. Certain of the recognized concomitants of chronic arsenical poisoning should be present, such as eczema, waxy pallor, blepharitis and a garlic odor of the perspiration.

Kraetzer further stated that it must be strictly understood that any conclusions derived from a case thus investigated pertain only to that particular case.

Regarding the first condition, it is difficult to see why the mere chance of contamination with arsenic from outside sources would not be sufficient. Indubitably, the greatest obstacle to be overcome in the arsenic problem is the lack of knowledge of the distribution of arsenic, and, even though one is aware of the presence of arsenic in the patient's body, further intake continues because one does not know how to shut off the source of supply. Certainly, one should not discard the possibility of arsenic poisoning in a given case merely because there is no history of definite exposure.

The quantitative demonstration of arsenic in the urine is a valuable aid in the diagnosis. However, the amount of arsenic in the urine, which may vary from day to day, need not be above that which is generally conceded to be "normal," because no fixed quantity of arsenic will produce disease in every person, and therefore no tolerance limit can be set. Consequently, if the amount of arsenic taken into the body is relatively unimportant from the standpoint of its ability to produce disease, surely the amount excreted in the urine is likewise unimportant.

The third postulate, that cure of the disease must follow the administration of sodium thiosulphate in order to identify arsenic as the cause of the symptoms, represents an optimistic attitude regarding the

value of sodium thiosulphate and perhaps is unfair to the drug itself. Although the value of sodium thiosulphate as a detoxicating agent in cases of poisoning due to arsenic and other heavy metals is on a rather secure basis, it is not known how this action is brought about. Furthermore, many physicians are skeptical of its actual value. Certainly, in severe cases of hepatitis or neuritis from arsenic poisoning, one expects little aid from the drug. In a case of dermatitis from one of the arsphenamines, sodium thiosulphate occasionally gives spectacular results and probably has reduced the mortality and the length of hospitalization. However, in many cases the drug is not effective, for unless it is given in the early stages of the disease it seems to be of little or no value. Furthermore, clinical evidence seems to indicate that the continued use of sodium thiosulphate aggravates arsphenamine dermatitis, and that the drug itself is capable of producing an exfoliative dermatitis.[7] Patients with arsenical pigmentation and arsenical keratosis of the palms and soles certainly are not benefited by the use of sodium thiosulphate, nor are patients with optic atrophy following the use of the trivalent arsenical drug tryparsamide benefited by it. However, failure of a given patient to respond to treatment with sodium thiosulphate does not rule out an arsenical etiology of the condition since irreparable damage may have been sustained, for instance, by the nerve tissue.

The fourth postulate, regarding the presence of symptoms recognized as coincident with chronic arsenical poisoning, is reasonable. However, at the present time it is impossible to evaluate the total destructive influence on human health which results from the widespread use of arsenic. Perhaps the future will disclose that other obscure diseases and symptoms are due to the presence of arsenic in the body. Witness Throne and Myers,[2c] who several years ago concluded that in about 30 per cent of cases of eczema arsenic is a factor of great importance. Other diseases mentioned in the literature in which arsenic is considered to be a possible factor are peripheral neuritis, hepatitis, disturbances of vision, obscure neurologic conditions, keratosis, cancer of the skin, alopecia areata, acrodynia, scleroderma and Raynaud's disease. Vogel [3a] reported that arsenic was found in sixty-nine of one hundred patients whose excretions were tested for arsenic. Since only thirty-four of the patients had been treated with arsenicals, in thirty-five cases the arsenic had entered the body in some unknown way. Forty of the one hundred patients had jaundice. The tests on thirty-four patients in this group of forty showed the presence of arsenic, but only six had been given arsenical medication. Therefore, in twenty-eight of the patients with jaundice there was no explanation for the presence of

7. Shelmire, B., in discussion on Shaffer, L. W.: Treatment of Postarsphenamine Dermatitis, Arch. Dermat. & Syph. **29**:187 (Feb.) 1934.

the arsenic. Other findings that may be offered as evidence that arsenic is an etiologic factor in a given case are: the presence of arsenic in the tissue as revealed by microchemical stains, recurrence of the symptoms on further contact with arsenic and a positive patch test.

Staining of a biopsy specimen for arsenic according to the method of Osborne [3n] gives valuable evidence and is especially practicable in questionable cases of arsenical dermatitis. Recently, however, Tannenholz and Muir [8] cast considerable doubt on the specificity of this method. They tried other methods, but the results were inconclusive, and the authors expressed the opinion that at present there is no reliable method of demonstrating arsenic in the tissues by microchemical means.

Causing the recurrence of symptoms by further contact with arsenic is not a practical method of determining the etiologic rôle of arsenic in a given case, since the serious nature of arsenical poisoning precludes the deliberate administration of the drug. In cases of arsenical eruptions the patch test has been shown to be an excellent method of determining cutaneous hypersensitiveness.[9] The usefulness of patch tests, however, is limited to cases in which there are cutaneous manifestations of arsenic poisoning or hypersensitiveness.

SUMMARY

A report is made of a probable case of arsenical dermatitis caused by wearing a black woollen suit. Arsenic was found in the urine and in the hair of the patient and in the woollen suit. Recovery occurred when the patient discontinued wearing the suit and when local treatment of the skin was instituted.

The presence of arsenic in excretions is discussed. Because arsenic is not known to be a necessary constituent of normally functioning tissues, the finding of the drug in the body in its excretions cannot be considered as normal even though arsenic is present in a large number of normal persons. The elimination of arsenic in any amount may be of clinical significance and should always be regarded with suspicion.[3m]

There are no definite criteria by which to identify arsenic as a cause of disease in a given case. At the present time the diagnosis in obscure cases of arsenical poisoning rests on presumptive evidence.

A general rule regarding the behavior of arsenic within the body is of little value because in many persons the biochemical reactions are exceptional. Patients who suffer from symptoms of arsenic poisoning are exceptions in that they manifest a hypersensitivity to arsenic.

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8. Tannenholz, H., and Muir, K. B.: Methods for Microchemical Demonstration of Arsenic in Tissues, Arch. Path. **15**:789 (June) 1933.

9. Schoch, A. G.: The Patch Test and the Element of Syringe Contamination in Arsphenamine Sensitization Dermatitis, J. A. M. A. **98**:1367 (April 16) 1932.

Legally, it is difficult to state whether or not arsenical poisoning has been the cause of death even though the amounts of arsenic found in the tissues and excretions are the same or less than those cited as "normal" values.

The use of arsenic as a contaminating factor in foods or drugs should not be permitted since no limit of tolerance for arsenic can be established for all persons.

REACTIONS TO TRICHOPHYTIN COMPARED WITH REACTIONS TO OTHER BACTERIAL PRODUCTS

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REACTIONS TO SIMULTANEOUS INTRADERMAL INJECTIONS OF MEASURED AMOUNTS OF TRICHOPHYTIN AND VARIOUS VACCINES

Intradermal injections of trichophytin and other bacterial products are in general use. It occurred to us to try simultaneous intradermal injections of more than one such product in the same person.

In ordinary practice the amount of trichophytin or bacterial vaccine injected is measured in fluid bulk. The technician uses 0.1 cc. of a definite dilution. In this series of studies it was decided to use another method of measurement. The nitrogen content of trichophytin and various bacterial products has been measured, but as far as we know no one has previously used equivalent amounts of nitrogen in various products for intradermal diagnostic injection as a basis for the comparison of reactions.

Equivalent Volume.—Table 1 gives the reactions of two patients to a series of intradermal injections of trichophytin and other bacterial products and the amount of nitrogen in each product. For these two patients 0.1 cc. of test material was used.

TABLE 1.—*Reactions to Simultaneous Injections of 0.1 Cc. of Various Products with Varying Nitrogen Content*

Material Injected	Mg. of Nitrogen in Each 0.1 Cc. of Product Injected	Reaction of Patient Forty-Eight Hours Later	
		S.	D.
Trichophytin (1)*	0.0166	+	—
Trichophytin (2)†	0.0120	++++	—
Streptococcus-staphylococcus vaccine‡	0.0056	++	—
Streptococcus-staphylococcus-bacillus vaccine‡	0.0056	++	—
Typhoid vaccine§	0.0084	+++	—
Typhoid-paratyphoid vaccine§	0.0112	+++	—
Gonococcus vaccine§	0.0030	+++	—
Control#	0.0100	—	—

* This is a multi-organism commercial product.
† This is a mono-organism product of the laboratory of the Stuyvesant Square Hospital.
‡ The streptococcus-staphylococcus vaccine and streptococcus-staphylococcus-bacillus vaccine are products of the laboratory of the Stuyvesant Square Hospital.
§ The typhoid, typhoid-paratyphoid and gonococcus vaccines were from the laboratory of the New York City Department of Health.
# The control was the broth culture medium.

From the service of Dr. Herman Goodman at the Stuyvesant Square Hospital, formerly the New York Skin and Cancer Hospital.

TABLE 2.—*Reactions to Simultaneous Intradermal Injections of Products with An Equivalent Nitrogen Content*

Patient	Clinical Diagnosis	Results of Microscopic Examination for Tinea	Results of Culture for Tinea	Material Injected: Trichophytin (1) (Nitrogen, 0.0116 Mg.)	Trychophytin (2) (Nitrogen, 0.012 Mg.)	Typhoid Vaccine (Nitrogen, 0.012 Mg.)	Typhoid-Paratyphoid Vaccine (Nitrogen, 0.0112 Mg.)	Streptococcus-Staphylococcus Vaccine (Nitrogen, 0.0112 Mg.)	Streptococcus-Staphylococcus-Coli Vaccine (Nitrogen, 0.0112 Mg.)	Gonococcus Vaccine (Nitrogen, 0.0092 Mg.)	Control (Nitrogen, 0.01 Mg.)
C. M.	Acne	—	—	—	—	—	+ —	—	—	—	—
C. J.	Eczema	—	—	—	+?	+ —	+ —	—	—	—	—
S. M.	Pruritus	—	—	—	+	+ —	—	+ —	+ —	+ —	—
A. H.	Alopecia	—	—	—	+ —	+	+	+	+	+	—
L. L.	Eczema	—	—	—	+	+	+	++	+	+	—
Y. R.	Tinea	—	—	—	+	+	+	+	+ —	+	—
C. T.	Paronychia	—	—	+ —	+	+ —	+	+ —	++?	+ —	—
J. B.	Tinea	—	—	+ —	++	+ —	+ —	+	+	+	—
C. K.	Dermatitis	—	—	+	++	+	?	+	+?	+ —	—
L. S.	Tinea	+	+	+	+	+	+ —	+	+ —	+	—
B. B.	Intertrigo	?	—	+	+	+	+	+	+ —	+	—
P. W.	Tinea	+	+	+	++	++	+++	+	++	—	—

TABLE 3.—*Reactions to Simultaneous Intradermal Injections of Increasing Amounts of Trichophytin and Bacterial Vaccines Measured According to the Nitrogen Content*

Patient	Material Injected: Trichophytin: Nitrogen, 0.0116 Mg.	Trichophytin: Nitrogen, 0.0232 Mg.	Trichophytin: Nitrogen, 0.0348 Mg.	Streptococcus-Staphylococcus Vaccine: Nitrogen, 0.0112 Mg.	Streptococcus-Staphylococcus Vaccine: Nitrogen, 0.0224 Mg.	Streptococcus-Staphylococcus Vaccine: Nitrogen, 0.0336 Mg.	Typhoid-Paratyphoid Vaccine: Nitrogen, 0.1120 Mg.	Typhoid-Paratyphoid Vaccine: Nitrogen, 0.0224 Mg.	Typhoid-Paratyphoid Vaccine: Nitrogen, 0.0336 Mg.	Control: Nitrogen, 0.0100 Mg.	Control: Nitrogen, 0.0200 Mg.	Control: Nitrogen, 0.0300 Mg.
C. T.	—	—	—	+	+	+						
C. J.	—	—	—	..	..	..	+++	+++	+++			
S. M.	+ —	—	—	+	+	+						
J. B.	+	+	+	..	..	..	..	..	..	—	—	—
C. K.	+	++	++	..	..	..	..	..	..	—	—	—
L. S.	+	+	+	..	..	..	..	..	..	—	—	—
B. B.	+	+	+	..	..	..	..	..	..	—	—	—
L. L.	—	—	—	..	..	..	..	..	..	—	—	—
S. S.	++	+++	+++	..	..	..	+++	+++	+++			
Y. R.	+ —	+	+	..	..	..	..	..	..	—	—	—
C. M.	+ —	+ —	+ —	..	..	..	..	..	..	—	—	—

The nitrogen content of 0.1 cc. of trichophytin (1) is in contrast to that of 0.1 cc. of the gonococcus vaccine.

Equivalent Nitrogen Content.—Table 2 gives the reactions of twelve patients to a series of simultaneous intradermal injections of trichophytin and other bacterial products so diluted that equivalent or almost equivalent amounts of nitrogen were injected with each product. The actual amount of nitrogen injected is given.

It should be noted that the reactions to the two samples of trichophytin were not the same in each patient.

All the materials injected in this series of tests were cultured for bacterial contamination and on Sabouraud's medium. There was no growth in any of the cultures.

A Widal test was done on each of the patients. P. W., who gave a strongly positive reaction to the intradermal injection of typhoid vaccine and a very strongly positive reaction to the intradermal injection of typhoid-paratyphoid vaccine, said that she had had typhoid fever in her youth. The reaction to the Widal test was strongly positive in dilutions from 1 : 40 to 1 : 160.

Increasing and Decreasing Nitrogen Content.—Another series of simultaneous intradermal tests was carried out, increasing amounts of vaccine, as measured by the content of nitrogen, being used.

The reactions obtained from this series of intradermal injections of increasing amounts of trichophytin and bacterial products according to the nitrogen content led to another test. Simultaneous intradermal injections of diminishing amounts of these products were made. We used both of our trichophytin products, with the results shown in table 4.

TABLE 4.—*Reactions to Simultaneous Intradermal Injections of Decreasing Amounts of Commercial and Laboratory Trichophytin Measured According to the Nitrogen Content*

	Material Injected					
	Trichophytin (1)			Trichophytin (2)		
Patient	Nitrogen, 0.0120 Mg.	Nitrogen, 0.0080 Mg.	Nitrogen, 0.0040 Mg.	Nitrogen, 0.0120 Mg.	Nitrogen, 0.0080 Mg.	Nitrogen, 0.0040 Mg.
L. C.	++	+	+	+++	++	++
I. A.	—	—	—	—	—	—
W. J.	—	—	—	+—	—	—
A. R.	—	—	—	+—	+—	—
C. K.	—	—	—	+—	+—	—
S. S.	—	—	—	—	—	—
C. M.	—	—	—	—	—	—

Summary.—When fluid trichophytin and a diversified series of bacterial vaccines in equal amounts were simultaneously injected intradermally into two patients, after forty-eight hours one patient had reacted to all, and the other to none, of the injected materials.

When fluid trichophytin and a diversified series of bacterial vaccines in doses containing equivalent weights of nitrogen were injected simultaneously into twelve patients, the indication was that although some patients react indiscriminately to many such products there is an indicated selectivity on the basis of which the weight of the nitrogen alone cannot be said to be the cause of the local reaction to intradermal reactions.

All the readings of the local reactions were taken no sooner than forty-eight hours after the injections.

In making the intradermal injections, individual syringes were used for each product. We made all the injections and took all the readings.

REACTIONS TO SIMULTANEOUS INTRADERMAL INJECTIONS OF MEASURED AMOUNTS OF TUBERCULIN AND TRICHOPHYTIN

Reference is occasionally found in the literature to comparisons of the local reactions to tuberculin and those to trichophytin injected intradermally. We thought that it would be worth while to try simultaneous intradermal injections of these two products in the same person; we used the conventional technic and the usual dilution and dosage. As the work proceeded, modifications were tried. All are duly recorded.

TABLE 5.—*Comparison of the Reaction to Simultaneous Intradermal Injections of Tuberculin According to the Mantoux Test and the Reactions to Skin Test Dilutions* of Trichophytin*

Patient	Old Tuberculin, 1:1,000, 0.1 Cc.†	Skin Test Dilution of Trichophytin‡		
		0.5 Cc.	0.1 Cc.	
1	—	—	—	
2	—	—	—	
2 (Repeat)	—	—	—	
3	+	—	—	
3 (Repeat)	..	—	+	
4	++	—	—	
5	++	— (Boiled trichophytin)§		
6	++	+ (Boiled trichophytin)		
7	++	—	++	
8	++	+	+	(Procaine hydrochloride)
9	++	++	++	
10	++	++	++	
11	++	++	++	
12	+++	+	++	
13	+++	++	++	
14	++++	+	+	
15	++++	+	++	
16	++++	+	++	
17	++++	+++	++	
18	++++	++++	+++	
18 (Repeat)	..	..	++	(Procaine hydrochloride)

* Procaine hydrochloride instead of a saline solution was used as a diluent in two tests.
† The old tuberculin from the department of health was diluted with a saline solution.
‡ The commercial trichophytin was diluted 1:100 with a saline solution for the skin test.
§ The boiled trichophytin was used in several tests of this series. It had previously been heated for five minutes at 100 C.

Effect of Boiling.—We gave a few patients injections of old tuberculin, boiled old tuberculin, trichophytin and boiled trichophytin. We had previously confirmed the thermostability of trichophytin.

TABLE 6.—*Comparison of the Reaction to Simultaneous Intradermal Injections of Boiled and Unboiled Tuberculin and the Reaction to Boiled and Unboiled (Thermostable) Trichophytin*

	Material Injected			
	Old Tuberculin (Mantoux), 0.1 Cc.		Skin Test Dilution of Trichophytin, 0.1 Cc.	
Patient	Unboiled	Boiled	Unboiled	Boiled
19	—	—	—	—
20	+++	++	—	—
21	+++	++	—	—
22	+++	+++	—	+—
23	+++	++++	+—	+

Equivalent Nitrogen Content.—We injected tuberculin according to the amount of nitrogen which we measured. The nitrogen content of the tuberculin was estimated to be from 0.004 Gm. to 0.1 cc. of a 1:1,000 dilution. In other words, when we did the Mantoux test we injected 0.004 Gm. of nitrogen. We injected varying amounts of trichophytin, as shown in table 7, and gave injections to two controls—to one an injection of the broth culture medium (negative control) and to the other an injection of typhoid-paratyphoid vaccine.

TABLE 7.—*Comparison of the Reaction to Simultaneous Intradermal Injections of Old Tuberculin (Mantoux) in Volumes According to Measured Amounts of Nitrogen and That of Trichophytin and Typhoid-Paratyphoid Vaccine in Volumes According to Varying Amounts of Nitrogen*

	Material Injected				
	Old Tuberculin (Nitrogen, 0.004 Gm.)	Trichophytin			Typhoid-Paratyphoid Vaccine (Nitrogen, 0.0112 Gm.)
Patient		Nitrogen, 0.004 Gm.	Nitrogen, 0.0154 Gm.	Nitrogen, 0.0308 Gm.	
24	—	—	—	—	—
25	—	—	—	—	—
26	++	—	—	—	—
27	++	—	—	—	+
28	++++	—	—	—	++++
29	++++	—	—	—	++++

The control (broth medium) never caused a local reaction.

All the reactions were read no sooner than forty-eight hours after the injections.

Equivalent Volume.—We practically repeated this experiment in comparison, but used conventional test doses instead of measuring the amount of nitrogen as a guide to the volume injected. The results are given in table 8.

TABLE 8.—*Comparison of the Reaction to the Simultaneous Intradermal Injection of Skin Test Doses of Old Tuberculin (Mantoux), Trichophytin and Typhoid-Paratyphoid Vaccine*

	Material Injected			
		Trichophytin, Skin Test Dilution of 1:100		
Patient	Old Tuberculin (Mantoux)	0.1 Cc.	0.2 Cc.	Typhoid-Paratyphoid Vaccine, 0.1 Cc.
30	—	—	—	— +
31	+	—	--	+
32	++	—	—	+ —
33	++	—	+ —	+

Extent of Reinjection.—We made a few observations on a feature of injections in intradermal tests which interests us very much. To a few patients who gave no local reaction to the intradermal injection of old tuberculin or trichophytin at the forty-eight hour interval we gave reinjections at the old site; we used a new site for control.

TABLE 9.—*Comparison of the Reactions to the Simultaneous Intradermal Injection of Skin Test Doses of Old Tuberculin (Mantoux) and of Trichophytin and Reinjection at the Site of the Negative Reaction to Both Injections*

	Material Injected					
	Old Tuberculin			Trichophytin		
Patient	First Injection	Second Injection at First Site	Injection at New Site	First Injection	Second Injection at First Site	Injection at New Site
34	—	—	—	—	—	—
35	—	++	+	—	—	—
36	—	++	++	—	—	—

Summary.—In these experiments we compared the reactions to local intradermal injections of old tuberculin (Mantoux) and those to commercial trichophytin in varying doses and under various conditions.

Under the conventional clinical conditions for the test, skin test doses being used as a routine in a group of unselected cases, we noted that no patient who gave a negative reaction to old tuberculin gave a positive reaction to trichophytin. The contrary was not observed in this series, for patients with negative reactions to trichophytin gave positive reactions to old tuberculin.

We noted that the more strongly positive reactions to old tuberculin were accompanied by the more strongly positive reactions to trichophytin in the same patient.

We found that the nitrogen content of a skin test dose of old tuberculin (Mantoux) was 0.004 Gm. and that positive reactions were elicited

by it. Test doses of trichophytin containing equivalent amounts of nitrogen caused no reaction, although the results in this series were inconclusive.

We found in a small series of three patients who at first gave negative reactions to old tuberculin and trichophytin that in two cases when reinjections with the same material were made at the same site or at another site a reaction was elicited forty-eight hours later. This observation is not new.

All the readings were taken no sooner than forty-eight hours after the intradermal injection. Temporary, evanescent superficial erythema reported by patients was not considered a reaction.

Individual syringes were used for each product in all the intradermal injections. The dilutions were made on each day of the testing from the same stock bottles for the duration of this study. We made the injections and took all the readings.

REACTIONS TO INTRADERMAL INJECTION OF TRICHOPHYTIN AT ONE SITE AND SIMULTANEOUS INTRADERMAL AND SUBCUTANEOUS INJECTIONS OF TRICHOPHYTIN AT ANOTHER SITE

It is generally agreed, and we have consistently found it true in our work, that the amount of trichophytin which gives a reaction when injected intradermally does not excite a reaction if given subcutaneously. We have accepted it as a fact that the subcutaneous injection of test doses of trichophytin does not cause any local visible reaction.

We made a series of injections according to the following outline:

1. The patient received an injection of a test dose of commercial trichophytin intradermally on the upper part of the right forearm. This is the conventional intradermal diagnostic injection of trichophytin.

2. The same patient received an injection of a test dose of commercial trichophytin subcutaneously at another site on the right forearm, and immediately afterward another test dose was injected intradermally above the subcutaneous injection.

3. On the upper part of the left forearm of the same patient we injected our broth control, to which no patient in our series gave a positive reaction.

4. As a further control experiment, at another site on the left forearm we injected a test dose of broth control subcutaneously, and immediately thereafter another injection of the broth control was made intradermally above the subcutaneous injection.

No patient of this new series gave a reaction to the broth control, either when receiving an intradermal injection or when receiving both a subcutaneous and an intradermal injection at the same site simultaneously.

TABLE 10.—*Comparison of the Reactions to the Intradermal Injection of Trichophytin in Skin Test Doses and Those to Simultaneous Intradermal and Subcutaneous Injections at the Same Site*

Patient	Intradermal Injection	Intradermal Injection of Trichophytin Over Site of Subcutaneous Injection
1	—	—
2	—	—
3	Ecchymosis	Ecchymosis
4	?	+
5	+	++
6	+	++
7	+	++
8	++	+++

Summary.—Two patients who gave negative reactions to the conventional test dose of trichophytin injected intradermally gave negative reactions to the simultaneous intradermal and subcutaneous injections at another site. The presence of the trichophytin subcutaneously did not cause a local reaction to the test dose injected intradermally.

Four patients who had one or two plus local reactions to the intradermal injection of trichophytin gave an increased local reaction at the site of simultaneous intradermal and subcutaneous injections.

It seems feasible that the increase in the reaction to subcutaneous and intradermal injections of trichophytin may have been due simply to the aggregate amount of the two quantities of trichophytin.

THE INFLUENCE OF PHENOL IN REACTIONS TO THE INTRADERMAL INJECTION OF TRICHOPHYTIN, OLD TUBERCULIN AND OTHER BACTERIAL PRODUCTS

There are a few references in the literature to the influence of the phenol content of trichophytin and other bacterial vaccines on the local reaction to intradermal injections of these products. Phenol is used in the preparation of old tuberculin. We thought that it would be worth while to make quantitative estimates of the phenol content of the various materials used by us for intradermal injection and to determine the influence of phenol (if any) on the local response to intradermal injections.

TABLE 11.—*Actual Amount of Phenol Injected with Each Product Utilized in the Intradermal Tests Reported*

Product	Phenol, Mg.	Nitrogen, Mg.
Trichophytin (1)	0.0006	0.0116
Trichophytin (2)	0.0007	0.0120
Streptococcus-staphylococcus vaccine	0.0680	0.0112
Streptococcus-staphylococcus-bacillus coli vaccine	0.0680	0.0112
Typhoid vaccine	0.0400	0.0120
Typhoid-paratyphoid vaccine	0.0250	0.0112
Gonococcus vaccine	0.0840	0.0092
Control	0.0000	0.0100

A new series of control experiments was done. Some of the patients who had been studied previously were recalled, and the intradermal injections were repeated, the plain broth, the broth with phenol added and phenol in saline solution being used as controls.

Fourteen patients received injections of the new series of control products. Forty intradermal injections were made. Only two doubtful reactions were noted in this series. One was to the injection of plain broth, and the other to the injection of phenol in a saline solution.

Summary.—A series of injections intended to show the influence of the presence of phenol on the reactions to the intradermal injection of trichophytin, old tuberculin and other bacterial products was made. The patients gave a negative or, rarely, a doubtful response to the introduction of broth, broth and phenol and phenol in a saline solution.

CONCLUSIONS

Patients may react to one or many bacterial products injected intradermally, and this reaction is not proportional to the nitrogen content of the injected material. The reaction must be dependent on other factors. These findings are in accord with those reported by other authors.

The reactions to the intradermal injection of old tuberculin and the simultaneous injection of trichophytin could not be compared on the basis of the nitrogen content alone.

When the reactions to the simultaneous subcutaneous and intradermal injection of trichophytin at the same site are greater than those to the intradermal injection alone, it may be due to the added trichophytin present.

The presence of phenol in the amounts usually added as a preservative for bacterial products has no influence on the local reactions to the intradermal injection of trichophytin, old tuberculin and other bacterial products.

Dr. Else Barthel and Miss Elinor Whitney of Dr. Jessup's laboratory and the members of Dr. Myer's laboratory at the hospital assisted us in the technical part of this work.

Dr. Marion Sulzberger reviewed these papers in manuscript form and made many helpful suggestions.

ACNE AND FURUNCULOSIS

PRELIMINARY REPORT OF TREATMENT WITH PHYSIOLOGIC SOLUTION OF SODIUM CHLORIDE LOCALLY OR BY INTRAVENOUS INJECTION

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For five or six years I have studied the results of chemical analyses of the blood of patients reporting to the outpatient department of the Stuyvesant Square Hospital.

A relationship which is not generally stressed was disclosed by a tabulation of the sugar and the salt content of the blood. As the average sugar content decreases, the salt content increases. Although the relationship is not absolute, it is fairly constant. The converse can be supported: As the average salt content of the blood increases, the average sugar content decreases. In this report no explanation for this reciprocal relationship is offered.

Sodium chloride is useful in therapy for many conditions. Baths of sodium chloride are recommended as a home remedy. Poultices of sodium chloride are prescribed. Surgeons have given infusions of solution of sodium chloride for shock. Recently, capsules of sodium chloride have been prescribed to prevent cramps on exertion. Physiologic solution of sodium chloride has been introduced intravenously for the relief of pustular skin eruptions due to the ingestion of bromide or iodide. For the past three years, an experimental study has been made of the effect of intravenous and local injection of physiologic solution of sodium chloride for the relief of pustular acne and furunculosis.

REPORT OF A CASE

M. H., a woman of 21 years, unmarried, native-born, was examined on Oct. 3, 1931. The skin of the face was covered with pustules of various sizes intermingled with papules. The skin was markedly reddened. The cheeks and chin were more thickly covered with the pustules than was the forehead. Many comedones were present.

At first glance the cutaneous condition appeared to be acne caused by the ingestion of bromide. An intravenous injection of physiologic solution of sodium chloride was given. The patient was told to bring copies of her prescriptions on the next visit. When she returned the skin had cleared very much as far as the pustulation was concerned. Another intravenous injection of physiologic solution of sodium chloride was given. The patient failed to bring the prescriptions, but was to do so on her next visit. By the time she brought the copies the skin had been completely relieved of the pustular element. The prescriptions were for calcium sulphide and not for bromide or iodide preparation. The sodium chloride was the means by which the pustular element was eradicated as no other treatment was given. When the skin first showed extreme redness, local dressings

of a solution of boric acid were advised, but they were soon discontinued. Local injections of physiologic solution of sodium chloride were made into any recalcitrant pustules. Intravenous injections were continued over a period of five months. During this time, the patient made thirty-three visits to the clinic. The solution administered was made up fresh of 2 Gm. of sodium chloride in 200 cc. of distilled water. The dose of 100 cc. was gradually increased to 200 cc.

The patient's blood gave a negative reaction to the Wassermann test. The urinary findings were of no importance. On October 7, 8 and 12 the patient received 100 cc. of a 1 per cent solution of sodium chloride. On October 15 a clinical analysis of the blood showed: urea nitrogen, 14.5 mg. per hundred cubic centimeters; uric acid, 3.5 mg.; sugar, 97.6 mg., and chloride, 503.3 mg. On March 3 no injection having been given for several weeks, the patient was given 200 cc. of a 1 per cent solution of sodium chloride intravenously. The chemical analysis of the blood immediately before the injection revealed 416.8 mg. of chlorides. The blood chloride level five minutes after the injection was 475.8 mg.

The patient was presented before the Section of Dermatology and Syphilology of the New York Academy of Medicine on March 10, 1932. At that time all signs of pustulation had disappeared. Some erythema was still present and some scarring.

COMMENT

The results of the treatment of this patient gave rise to the question of whether the results were accidental and whether they could be repeated.

Since this patient came under my care, I have treated several hundred patients with pustular conditions of the skin by the use of physiologic solution of sodium chloride administered intravenously and locally into the pustules. The pustular elements have always receded under this type of treatment. The large pus pockets of the condition sometimes called cystic acne have cleared and remained clear. Furuncles, likewise are amenable to this form of therapy. It seems to make no difference whether the furuncle is in the frank pustular phase or in the stage before ripening.

In the beginning, all patients with acne were treated intravenously. The first injection was 100 cc. which was increased by 50 cc. until a maximum of 250 cc. was reached. A few patients were given 300 cc. There were no ill effects. The injections were carried out by the gravity method. When the lesions of papular acne did not respond, the administration of physiologic solution of sodium chloride was limited to patients with frank pustular lesions. If the patient had only one or two pus pockets, the solution was injected locally, directly into the mass of pus. Injections were made around the inflammatory base as well. The amount varied with the quantity which could be injected. If there was an aperture in the pustule the solution acted as a means of irrigation. Injections were made around as well as into the open pustules. This was the technic used in the case of furuncles.

Recently Bloom reported excellent results in the treatment of certain skin conditions, including acne, from the use of calcium chloride

intravenously. Patients with pustular acne were relieved of the pus pimples when given intravenous injections of physiologic solution for such unrelated conditions as vascular diseases of the lower extremities.

The report that physical effort causes a loss of salt with perspiration may account for the presence of furunculosis in men in training, although it is difficult to understand why in men in the best of health furuncles should develop. This loss of salt may be due to the increase in the sugar content.

A short series of experiments with cultures has been carried out. Streptococci and staphylococci have been grown on mediums to which increasing percentages of salt have been added. A concentration between 2 and 3 per cent inhibits the growth of such bacteria.

The relation of a high sugar content to a low salt content may be found to be constant for other infections. One may recall that persons with frank diabetes are prone to have pustular infections of the skin. Intravenous injections of physiologic solution of sodium chloride may be indicated in such cases.

This is a preliminary report of the clinical experiences with the administration of intravenous and local injections of physiologic solution of sodium chloride in pustular acne and furunculosis. The results warrant further study and a wider application.

EXPERIMENTAL CHRONIC CUTANEOUS BLASTOMYCOSIS IN MONKEYS

A STUDY OF THE ETIOLOGIC AGENT

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The clinical term blastomycosis has been used to designate any disease caused by a yeastlike fungus. At the present time, however, there is a growing tendency to limit this term to those diseases in which the causative fungi occur in the lesions, without associated mycelium, as large, round to oval cells possessing well defined membranes, well marked double contours and granular cytoplasm and multiplying in the tissues by budding, though capable of producing hyphae in more or less abundance in cultures. In line with this conception it is customary to designate those diseases caused by other yeastlike fungi by more specific terms, such as coccidioidal granuloma, sporotrichosis, torulosis and cytomycosis.

It is now evident that the term blastomycosis is doubly a misnomer. It was applied under the mistaken impression (1) that the causative organism is a true yeast and (2) that Blastomyces instead of Saccharomyces is the correct scientific name for the yeasts. It is now known that the various species responsible for blastomycosis occur in the lesions not as true yeasts but only as yeastlike forms of higher fungi. As has been recently suggested by Ota and Kawatsure,[1] such yeastlike structures are to be regarded as chlamydospores. According to this view, with which I am in accord, the buds that develop in the tissues from the spherical cells represent the anlagen of hyphae which, owing to conditions of unfavorable environment, are unable to develop normally but, instead, form other chlamydospores.

It would seem that the reason the term blastomycosis is retained is that it includes a variety (etiologically speaking) of similar infections, the causative agents of which are fungi which are not thoroughly understood and the classifications of which are still unsettled. As the knowledge of these fungi is increased it may be possible to discard the term.

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1. Ota, M., and Kawatsure, S.: Zur Aetiologie der echten und falschen Blastomycosen, besonders der Gilchristschen Krankheit, Arch. f. Dermat. u. Syph. **169**: 173, 1933.

The first description of a parasite causing blastomycosis was published by Gilchrist [2] in 1896. Gilchrist regarded the yeastlike cells which he discovered in a cutaneous ulcer as plant parasites. A little later, Gilchrist and Stokes [3] established the fungous nature of an apparently identical parasite which they cultivated from the cutaneous lesions of another patient. In numerous reports since that time parasites with identical morphology as they occurred in skin have been held responsible for similar lesions, as well as for systemic, and combinations of cutaneous and systemic, lesions.

Castellani,[4] aided by Agostini,[5] has made cultural studies of numerous lesions of cutaneous and systemic blastomycosis. The results of these investigations indicate that, although apparently identical in the tissues, the incriminated parasites in reality represent a group of pathogenic fungi rather than a single infectious agent. Thus, Castellani [4] has described Geotrichum dermatitidis which he regards as identical with Blastomyces dermatitidis of Gilchrist and Stokes,[3] Monosporium tulanense (1926), Glenospora lanuginosa (1930), Geotrichum multifermentans (1933), Glenospora brevis (1933), Glenospora meteuropa (1933) and Glenospora metamericana (1933), all of which occurred as large yeastlike cells with double-contoured, highly refractile membranes in the lesions which they produced.

Other fungi reported as etiologic agents of blastomycosis are Endomyces capsulatus (Rewbridge, Dodge and Ayers,[6] 1929), Endomyces capsulatus var. isabellinus (MacBryde and Thompson,[7] 1933), Endomyces dermatitidis (Moore,[8] 1932), regarded by Moore as identical with the parasite originally described by Gilchrist and Stokes, and Scopulariopsis americana (Ota and Kawatsure [1]).

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2. Gilchrist, T. C.: A Case of Blastomycetic Dermatitis in Man, Johns Hopkins Hosp. Rep. **1**:269, 1896.

3. Gilchrist, T. C., and Stokes, W. R.: A Case of Pseudo-Lupus Vulgaris Caused by a Blastomyces, J. Exper. Med. **3**:53, 1898.

4. Castellani, A., and Jacono, I.: Observations on Fungi Isolated from Cases of Blastomycosis Cutis and Blastomycosis Pulmonalis in North America and Europe: Remarks on Blastomycetin, J. Trop. Med. **36**:297 (Oct. 16) 1933.

5. Agostini, A.: Observations on Fungi Found in Cases of North American Blastomycosis of the Skin and Lungs, J. Trop. Med. **35**:266 (Sept. 1) 1932.

6. Rewbridge, A. G.; Dodge, C. W., and Ayers, T. T.: A Case of Meningitis Due to Endomyces Capsulatus (New Species), Am. J. Path. **5**:349 (July) 1929.

7. MacBryde, C. M., and Thompson, E. J.: Meningitis and Dermatitis Caused by a New Variety of Blastomycete (Endomycete), Arch. Dermat. & Syph. **27**:49 (Jan.) 1933.

8. Moore, M.: Blastomycosis: Report of a Case, with a Study of an Etiologic Factor and a Classification of the Organism, Ann. Missouri Bot. Gard. **20**:79 (Feb.) 1932.

Mention should be made of Phialophora verrucosa (Thaxter,[9] 1915) and Acrotheca pedrosoi (Brumpt, 1921), because these fungi are held responsible for the cases of chromoblastomycosis that have been reported. In chromoblastomycosis, which differs in some of its clinical aspects from the more common form of cutaneous blastomycosis, the parasitic form of both the species just mentioned occurs in the lesions as large, double-contoured, yeastlike cells with refractile membranes. Their blackish-brown color differentiates them from the parasites that have been described in blastomycosis.

The important features of blastomycosis have been adequately presented by Ricketts,[10] Hektoen,[11] Montgomery and Ormsby,[12] Wade and Bel[13] and Moore.[8]

Coccidioidal granuloma has often been confused with blastomycosis, and differentiation between them must be accomplished in the laboratory. In the lesions of coccidioidal granuloma, Coccidioides immitis or, less frequently, its near relative Coccidioides esferiformis can usually be readily demonstrated in the tissues as the causative parasite. Although the consensus is that these organisms reproduce in the tissues only by endosporulation, in some cases it is impossible, or at least difficult, to demonstrate the characteristic asci in smears from the lesions of human beings. At times all of the parasitic forms encountered may be indistinguishable from nonbudding forms of one of the parasites responsible for blastomycosis. In such cases the identity of the fungus may be established following the inoculation of a suitable animal (preferably the mouse) with a culture of the mycelial form of the fungus, which is usually readily obtainable on any of the commonly used sugar mediums. One week after intraperitoneal injection the characteristic asci may be demonstrated in large numbers in pus from the lesions.[14]

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9. Thaxter, R., quoted by Medlar, E. M.: A Cutaneous Infection Caused by a New Fungus, Phialophora Verrucosa, with a Study of the Fungus, J. M. Research **32**:507, 1915.

10. Ricketts, H. T.: Oidiomycosis (Blastomycosis) of the Skin and Its Fungi, J. M. Research **1**:373 (Dec.) 1901.

11. Hektoen, L.: Systemic Blastomycosis and Coccidioidal Granuloma, J. A. M. A. **49**:1071 (Sept. 28) 1907.

12. Montgomery, F. H., and Ormsby, O. S.: Systemic Blastomycosis: Its Etiologic, Pathologic and Clinical Features as Established by a Critical Survey and Summary of Twenty-Two Cases, Seven Previously Unpublished. The Relation of Blastomycosis to Coccidioidal Granuloma, Arch. Int. Med. **2**:1 (Aug.) 1908.

13. Wade, H. W., and Bel, G. S.: A Critical Consideration of Systemic Blastomycosis, Arch. Int. Med. **18**:103 (July) 1916.

14. The results of experiments on animals indicate that at least four specimens previously reported as causative agents of blastomycosis are closely related to C. immitis. Thus, Benham (Benham, R. W.: The Fungi of Blastomycosis and

(Footnote continued on next page)

The diagnosis of blastomycosis is not always easy, especially in those cases in which there are no cutaneous lesions. A positive diagnosis usually depends on the finding of the yeastlike parasites in smears, biopsy sections or sputum. Recently I observed a case in which the parasites were first demonstrated in the exudate obtained by prostatic massage several weeks before cutaneous lesions developed. In my opinion cultures of material from lesions in which the parasites are so rare as to escape detection after thorough microscopic examination seldom yield positive results.

In most cases of cutaneous blastomycosis the diagnosis is not often made until the lesions have existed for a comparatively long period of time. Of the six patients with the condition treated in the Vanderbilt University Hospital and Dispensary during the past seven years, the average duration of the lesions before the diagnosis was made was six and one-half years. In one case the condition had been undiagnosed, or incorrectly diagnosed, for twenty years. There is no doubt that in some cases of blastomycosis in which only mild lesions occur the condition is cured by potassium iodide administered under the mistaken diagnosis of syphilis. As a result the apparent incidence of the disease is probably less than its real incidence.

In most cases of blastomycosis the condition appears in the form of skin lesions which in the early stages usually respond readily to treatment. Early diagnosis of the disease, therefore, is highly desirable, since proper treatment usually results in cure, and the patient is relieved of the hazard of the systemic infection with its much more serious prognosis.

In every case the parasites should be studied culturally and identified if possible, for, as already mentioned, several investigators have shown that fungi capable of producing the disease may belong to widely divergent botanical groups.

Most of the fungi that have already been tested in animals have proved on subcutaneous inoculation to be mildly pathogenic for rabbits and slightly more pathogenic for guinea-pigs. Cultures similarly injected into dogs and white rats have given rise to localized abscesses and

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(Footnote 14 concluded)

Coccidioidal Granuloma, Arch. Dermat. & Syph. **30**:385 [Sept.] 1934), in a recent paper, reported the formation of asci in guinea-pigs inoculated with Blastomycoides (Geotrichum) dermatidis, G. meteuropa and S. americana. With the first two species named and also with Geotrichum louisianoideum, all obtained directly from Castellani, I have obtained asci in mice following intraperitoneal inoculation. In all cases blood agar cultures of material from the lesions of the infected mice yielded mycelium without formation of asci. As in cultures of C. immitis, the mediums of these cultures rapidly assumed a greenish-black color, apparently due to the formation of methemoglobin. This discoloration of the medium may prove to be characteristic and of importance in differentiating members of this group from the species causing blastomycosis.

granulomatous lesions which soon healed. Occasionally there develops in white rats, and more often in white mice, rapidly fatal, generalized infections following intratesticular or intraperitoneal injection of the culture. Based on such results some investigators, when dealing with fungi isolated from lesions of cases of uncomplicated cutaneous blastomycosis, have made the unwarranted statement that Koch's postulates had been fulfilled. So far as I know, lesions analogous to the chronic cutaneous disease as it occurs in man have not heretofore been induced in any experimental animal.

From the lesions of a patient with cutaneous blastomycosis I have recently obtained a fungus which I have identified. By means of intra-

Fig. 1.—Photograph of the patient, showing the appearance of the lesions before treatment was initiated. The ulcer in the region of the occiput had been present for approximately nine years.

dermal and subcutaneous injection of cultures of this fungus I have succeeded in inducing cutaneous lesions in monkeys typical of the cutaneous disease in man.

REPORT OF A CASE

History.—J. G., a farmer, 68 years old, was admitted to the Vanderbilt University Hospital Dispensary on April 14, 1933, with a complaint of comparatively painless ulcers on the face and neck, some of which had been present for nine years. The patient was blind in the right eye.

About nine years previously two small boils had formed, one on the back of the neck and the other on the outer surface of the upper part of the right arm. They ruptured shortly and discharged blood-tinged pus. The resulting ulcers

increased in size and became chronic; that on the arm healed after about four years. Additional ulcers developed on the back of the head and neck, but complete healing never occurred.

During January and February 1933 the patient was forced to remain in bed on account of severe pain in the right eye; complete blindness in that eye ensued about three weeks before he came to the dispensary. Vision in the left eye was beginning to be impaired.

Physical Examination.—The patient was a fairly well preserved white man 68 years of age. On the back of the neck and extending well above the occiput was a large, pinkish, scarred area containing three large ulcers, one just behind the left ear, another at the occiput and the third just behind the right ear. They varied from 2 to 6 cm. in diameter. Each had slightly raised edges, and the weeping granulation tissue in the center was in part covered by a honey-colored crust. Extending from the lobe of the right ear across the right cheek was a verrucous lesion, likewise partially covered with crust, which involved both the upper and the lower lip and most of the chin on the right side. There was no appreciable enlargement of the cervical lymph nodes. On the right arm just below and lateral to the deltoid insertion was a large, irregular scar which covered an area of about 6 sq. cm. Examination of the eyes revealed bilateral cataracts with complete blindness in the right eye due to glaucoma.

Laboratory Examination.—Wassermann and Kahn reactions of the patient's blood were negative. Smears from the ulcers revealed numerous yeastlike cells with a doubly-contoured, highly refractile membrane. Sections removed for biopsy showed epidermal hyperplasia, numerous intradermal abscesses and chronic granulation tissue which contained numerous giant cells. There were parasites in large numbers in the giant cells and lying free within the abscesses. Dextrose agar cultures of washed bits of granulation tissue yielded the fungus employed in these studies.

Clinical Diagnosis.—The diagnosis was blastomycosis of the face and neck; glaucoma of the right eye and bilateral senile cataract.

Course.—The patient was given by mouth 25 drops of potassium iodide (saturated aqueous solution) three times daily. By August 4, approximately four months after treatment was begun, the ulcers had completely healed. There has been no recurrence of the cutaneous lesions since the patient's discharge almost one year ago.

ISOLATION OF THE FUNGUS

Small bits of granulation tissue were removed from the most active portion of the verrucous lesion on the face, thoroughly washed in several changes of 0.85 per cent saline solution and smeared on dextrose agar (p_H 6.5) plates and slants. The cultures were sealed and allowed to incubate at room temperature (from 25 to 28 C.). On the third day a few colonies of staphylococci (from one to six) were noted in all of the cultures, but not until sixteen days later could any fungous growth be discerned. At that time the colonies were approximately 1 mm. in diameter and consisted entirely of mycelial growth. This was followed by an abundance of white aerial hyphae which turned grayish brown with age. A few of the colonies reached a diameter of 4 cm., but most remained comparatively small, owing, no doubt, to the presence of the contaminating staphylococci. Although microscopic examination was made from time to time during the period of three months in which these primary cultures were observed, yeastlike forms of the fungus similar to those observed in the lesions in man were never seen.

CULTURAL DESCRIPTION OF FUNGUS

The fungus grows readily on dextrose agar (p_H 5.5 and 7.2). The growth at first is white and fluffy owing to the abundance of aerial hyphae. After about ten days the under surface becomes brownish, but the medium remains clear. After three weeks the aerial hyphae extend upward along the sides of the culture tube.

In plate cultures, if precautions are taken to prevent excessive drying of the medium the colonies frequently measure as much as 4 cm. in diameter at the end of the fourth week. The aerial hyphae gradually assume a grayish-brown color with age. Not infrequently radiating ridges and furrows develop like those seen in colonies of Trichophyton. The cultures likewise possess an odor similar to that of cultures of Trichophyton.

The fungus grows equally well on potato-dextrose agar (p_H 5.6) and somewhat less luxuriantly on infusion agar (p_H 7.2), mannitol agar (p_H 7.2), Sabouraud's agar (p_H 5.6), Czapek's agar (p_H 4.4) and potato. Otherwise, cultures on these mediums appear similar to those on dextrose agar. It also grows fairly well on 10 per cent rabbit blood agar, but aerial hyphae are scanty, the growth for the most part taking place in the substratum. On glycerin agar the growth is luxuriant, somewhat nodular and usually almost devoid of aerial hyphae; chlamydospores develop in abundance.

The fungus also grows well in infusion broth (p_H 7.2), with or without dextrose. In such a liquid medium the colonies grow as submerged masses of intertwining hyphae without discoloring the surrounding medium. The hyphae vary in width from 1.5 to 3 microns, averaging 1.7 microns. Numerous round to oval conidia, fairly uniform in size, and measuring 4.5 by 3 microns, are attached to the mycelium. Some of the conidia are sessile, but many are supported by well developed sterigmata which vary in length from 1 to 10 microns. Chlamydospores, both intercalary and lateral, are abundant. In old cultures these structures, which appear as thick-walled spherical cells from 8 to 15 microns in diameter, often become free and seem indistinguishable from the yeastlike forms of the fungus as they occur in the lesions. These chlamydospores form in greater abundance in broth culture containing a small amount (1 per cent) of human or rabbit serum.

In dextrose agar slide cultures clear, branched, septate hyphae approximately 1.5 microns in diameter begin to grow from the inoculum within forty-eight hours. Almost immediately thereafter conidia begin to appear in abundance on the older portion of the mycelium. Most of the conidia as they occur on the aerial hyphae are pyriform, but some are elongated and others have the shape of a distorted dumb-bell.

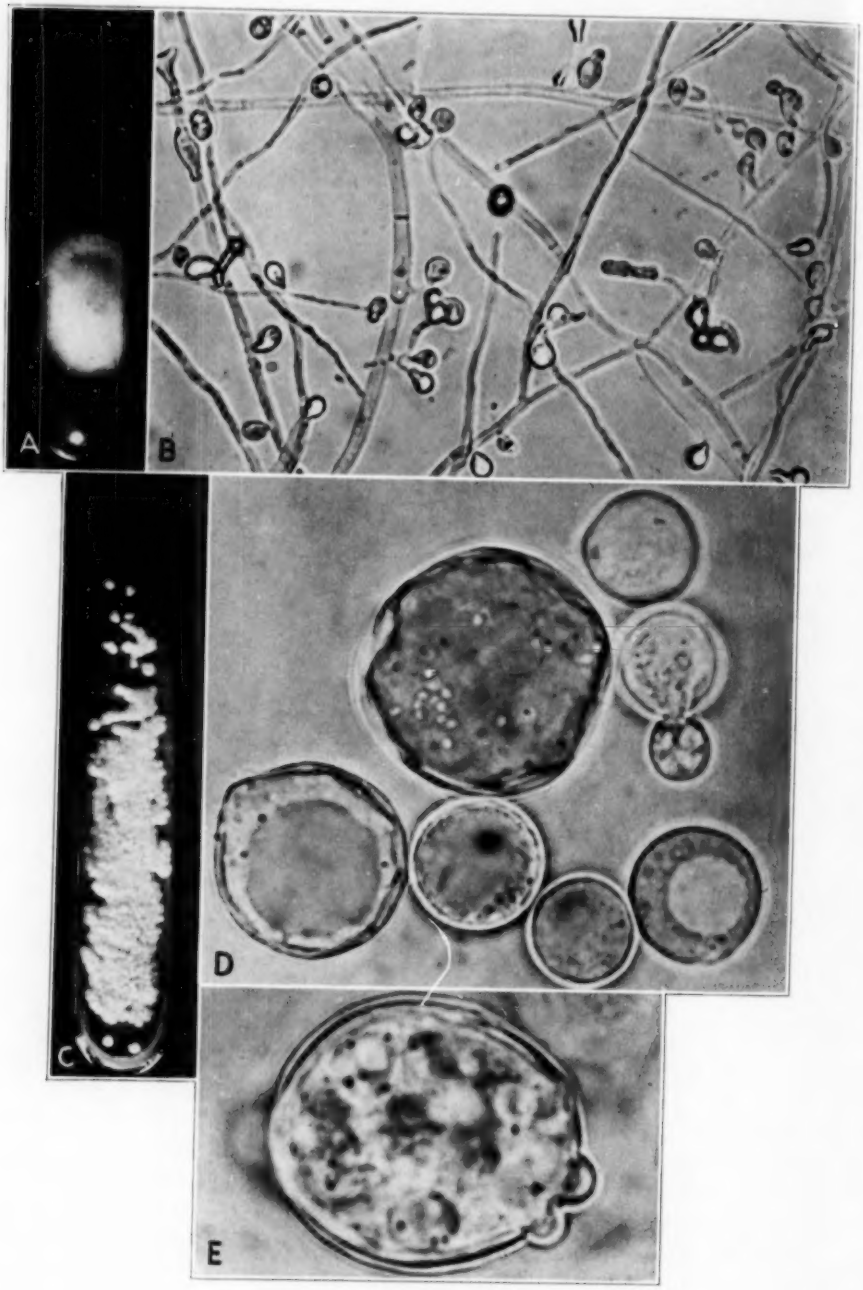

Figure 2

EXPLANATION OF FIGURE 2

Fig. 2.—*A* is a photograph of the mycelial form on dextrose agar, grown for eight days at 25 C. *B* is a photomicrograph (× 750) of aerial hyphae in a dextrose agar slide culture incubated fourteen days at 25 C. The hyphae are of two distinct sizes. Numerous conidia, usually pyriform, may be seen supported by short sterigmata. *C* is a photograph of the yeastlike form of the fungus grown on Petragagni's medium for eight days at 37 C. Compare with the mycelial form shown in *A*. The colonies are yellowish white and have rough surfaces. The growth appears dry and on the whole resembles cultures of the tubercle bacillus on this medium. The yeastlike form grows in a similar manner on rabbit blood agar, but the colonies appear somewhat brownish owing to absorption of coloring matter from the blood-containing medium. *D* is a photomicrograph (× 1,400) of yeastlike forms of the fungus from a blood agar culture incubated at 37 C. for five days. The two larger cells have well defined capsules. A third cell in line with these is beginning to acquire a thick membrane. Three other cells in the lower part of the picture still posssess a thin membrane, the clear zones surrounding them being due to an optical phenomenon. Note the large, well defined vacuoles within some of the cells. One budding form may be seen. *E* is a photomicrograph (× 2,000) of a large, thick-walled cell from the same blood agar culture, showing multiple buds. Two buds may be clearly seen; a third, not in focus, appears as a shadow. Observations of similar cells in slide cultures have convinced me that these structures are really buds and not simple extrusions of cytoplasm through defects in the membranes of old cells.

They are slightly larger than the conidia which develop in broth cultures, but in either case the manner of their attachment to the hyphae is the same, some being sessile while others are supported by short sterigmata. As the cultures grow older hyphae of two distinct sizes may be observed. One, the predominating filament, has a diameter of approximately 1.5 microns; the other, a diameter of approximately 4 microns. Conjugation and formation of asci have not been observed. In the submerged portions of the growth some of the hyphae increase in thickness and become segmented to form more or less spherical arthrospores from 10 to 15 microns in diameter. Later, chlamydospores similar to those which occur in broth cultures are also seen within the substratum.

The descriptions of this fungus, as recorded, have been obtained from cultures incubated at room temperature (approximately 25 C.). When cultivated at a higher temperature (from 28 to 38 C.) the growth is comparatively poor, and the colonies appear as tufts of short aerial hyphae surrounded by a peripheral zone of mycelium growing in and on the surface of the medium. The optimum temperature range lies between 20 and 25 C. Some growth, however, takes place at much lower temperatures. For example, at the time the original cultures were made of material from the lesion of the patient small bits of tissue from the lesion were placed on glass slides in small droplets of 0.85 per cent saline solution. After the application of cover-slips these preparations were sealed with petrolatum and placed in an electric refrigerator at a temperature of 8 C. Examination after thirty days revealed considerable development of mycelium originating from the yeastlike forms of the fungus contained in the human material. The hyphae contained an abundance of fat droplets like those of older cultures grown at a more favorable temperature. Conidial formation did not take place during the ten weeks that the cultures were observed.

The fungus is an aerobe. It produces neither acid nor gas in mediums containing dextrose, saccharose, maltose, lactose, mannitol, inosite, rhamnose, xylose or levulose. Milk is rendered slightly alkaline and is not coagulated. Slow liquefaction of gelatin begins to take place after three weeks.

IDENTITY OF FUNGUS

The characters outlined led me to believe that this species is closely related, if not identical, with M. tulanense (Castellani [4]). Dr. Castellani studied it in his laboratory in London and advised me that "the fungus seems to be morphologically and physiologically indistinguishable from the original Monosporium tulanense."

CULTIVATION OF THE TISSUE FORM OF THE FUNGUS ON ARTIFICIAL MEDIUMS

Although old cultures of the mycelial form of this fungus often contain chlamydospores and conidia which sometimes become detached from the mycelium to appear as free, somewhat spherical, cells indistinguishable from the yeastlike forms seen in lesions of blastomycosis, reproduction of these spores has never been observed on artificial culture mediums without an intermediate phase of hyphal development.

I have, however, by utilizing a method first successfully employed [15] in obtaining cultures of the tissue form of another fungus, Histoplasma capsulatum, succeeded in cultivating this fungus in its tissue form on artificial culture mediums. This method is based on the fact that the tissues of a susceptible animal have the power to convert the mycelial form of the fungus to the yeastlike or tissue form and that the latter form, when obtained from early lesions experimentally produced, tends under certain conditions to proliferate as such on mediums rich in protein, rather than to produce mycelium, as do similar forms derived from chronic lesions.

The method is as follows: Mycelium suspended in 0.85 per cent saline solution is injected intraperitoneally into a mouse. Forty-eight hours later the animal is killed and submerged in a solution of compound solution of cresol for five minutes. The abdominal viscera are then exposed aseptically. In practically every instance several small, soft, white nodules are found loosely attached to the peritoneal surface of the abdominal wall anteriorly or to the fatty tissue lying between the spleen and the stomach. One or more of these nodules are smeared on the surface of 10 per cent rabbit blood agar in Petri dishes and incubated at approximately 37 C. Usually after three days numerous dry, rough-surfaced colonies varying in size from 0.5 to 1 mm. and composed entirely of budding yeastlike forms of the fungus become apparent in the cultures. These colonies are easily removable from the surface of the medium, are quite friable and are light brown, owing to the absorption of coloring matter from the blood-containing medium. As a rule, colonies of the mycelial form of the fungus are also present in varying numbers.

Microscopic examination of the nodules removed from the mouse reveals fungous elements and inflammatory cells. When young cultures are used for the injection the mycelium is seen breaking up to form elongated cells with rounded ends. These cells rapidly become more or less spherical, develop thick membranes and in every particular assume the appearance of the yeastlike cells seen in lesions of blasto-

15. DeMonbreun, W. A.: The Cultivation and Cultural Characteristics of Darling's Histoplasma Capsulatum, Am. J. Trop. Med. **14**:93 (March) 1934.

mycosis in man. If older cultures containing an abundance of conidia and chlamydospores and many degenerated hyphal segments are used, large numbers of budding yeastlike cells are seen in the material removed from the animal after forty-eight hours. The presence of these cells in abundance in such early lesions indicates a close relationship between the spores in the cultures and the yeastlike forms that develop in the animal tissues.

The yeastlike forms in blood agar cultures are round to oval and vary in size from 4 to 25 microns, the average being 15 microns. In fresh preparations obtained from young cultures (from one to three days) the majority of the forms consist of relatively thin-walled cells, each of which in most instances contains a large vacuole. Lying between the vacuole and the cell membrane is a zone of protoplasm that contains numerous small fat droplets and protoplasmic granules. As these cells grow older there develops a double-contoured, highly refractile membrane, the vacuole tends to become inconspicuous, the fat droplets in the protoplasm increase in size and the protoplasmic granules often possess active brownian movement. When mounted in an 0.85 per cent solution of sodium chloride for forty-eight hours the cytoplasm is frequently seen as a contracted, granular mass separated from the cell membrane by a clear zone.

The greater part of the growth that takes place in cultures results from budding by the cells before the thick, double-contoured membrane develops. The older cells proliferate also by budding, but more slowly. In the latter the buds, sometimes as many as four on a single cell, appear as thinned-out areas of the cell membrane. After increasing in size they are set free like the buds of younger cells by the formation of a cross-wall which is formed by the pinching in of the cell membrane. Some of the young buds are set free from the mother cells when still quite small. As a rule these immature cells appear as small spheres from 4 to 6 microns in diameter with an easily discernible membrane and homogeneous cytoplasm. Occasionally, however, the membrane is so thin that the cell is detected with difficulty. In old cultures that have ceased growing practically all of the cells are seen to have a thick, double-contoured membrane. Such evolution indicates that the final form assumed by the yeastlike cell in blood agar cultures, under certain conditions, is the chlamydospore.

The yeastlike form of the fungus apparently can be carried on indefinitely on freshly prepared rabbit blood agar provided transfers are made at frequent intervals and precautions are taken to prevent excessive drying of the medium. It is essential that the temperature of incubation be approximately 37 C.; incubation at lower temperatures results in the development of hyphae. Likewise, the employment of mediums with a low protein content results in the development of

hyphae. When the yeastlike forms are transferred from blood agar to such mediums as dextrose agar, Sabouraud's agar, potato or broth, even when incubation is carried on at 37 C., they give rise to mycelium with the characteristics already described. If unsealed young blood agar cultures of the yeastlike cells are placed immediately after inoculation in a "dry" incubator at 37 C., or otherwise are allowed to dry out, most of the cells become oval to cylindric and there is a tendency to form chains of elongated cells. Such cells may be propagated in this form if transplants are made at frequent intervals on blood agar and incubated at 37 C. As such cultures grow older the cells acquire branching hyphae, indicating the beginning of mycelial formation. As in the case of cultures on this medium incubated at room temperature, growth takes place in the substratum. On continued incubation, however, scanty aerial hyphae form, giving the growth a "prickly" appearance. The tendency for the fungus to grow in the mycelial form is strong. In my experience, once this type of growth is initiated cultures of the yeastlike form cannot be regained by any manner of manipulation of the growth on artificial mediums. To obtain this form again in culture I have found it necessary to resort to the "mouse method" previously described.

The yeastlike form grows somewhat more luxuriantly on Petragagni's [16] medium (without malachite green) than on blood agar. However, I have given the foregoing descriptions as on the other medium because it may be prepared much more easily and the growth on it is sufficiently satisfactory.

REPRODUCTION OF CUTANEOUS AND SYSTEMIC BLASTOMYCOSIS IN MONKEYS

With cultures of the yeastlike form, lesions typical of cutaneous blastomycosis in man have been induced in two Macacus rhesus monkeys.

MONKEY 1.—This animal received, in the lower abdominal quadrants, two intradermal injections, each consisting of 0.05 cc. of a rich suspension of the yeastlike forms, and a single subcutaneous injection of 0.25 cc. Areas of redness appeared at the sites of the intradermal injections but disappeared after about forty-eight hours. About four weeks later areas of induration became perceptible at these sites, and the overlying skin appeared brown and scaly. As the lesions progressed they assumed the appearance of somewhat flattened nodules which after a time reached a diameter of 1 cm. when ulceration occurred. These nodules were confined to the skin and were freely movable with the skin.

At the site of the subcutaneous injection there appeared an area of induration which gradually became nodular. The nodule increased in size, and at the time it became ulcerated the superficial inguinal lymph nodes of each side were noticed

16. Norton, J. F.; Thomas, J. G., and Broom, Norma H.: Laboratory Tests for Tubercle Bacilli by Culture Methods, Am. Rev. Tuberc. **25**:378 (March) 1932.

to be enlarged. Approximately three months after the animal was inoculated these nodes broke down, and several sinuses which discharged a purulent exudate containing large numbers of the yeastlike cells appeared in the overlying skin. The general health of the animal remained good for an additional period of three months. It then took food very poorly and became greatly emaciated. A persistent hacking cough developed, and the animal died approximately eight months after being inoculated.

Autopsy revealed, in addition to the superficial lesions already described, a mass approximately 5 cm. in diameter in the balled-up omentum which lay between the spleen and the stomach. While it was being removed the mass ruptured, and thick pus escaped in abundance. The retroperitoneal, mesenteric and bronchial lymph nodes were considerably enlarged and fairly soft and on section were seen to contain numerous whitish-yellow nodules which varied in size from 1 to 5 mm. Some of the nodules were soft and appeared to be abscesses; others were firm and were indistinguishable from tubercles. The lungs were a mottled grayish

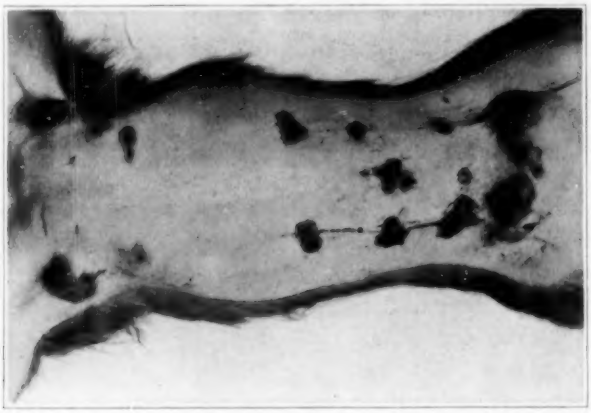

Fig. 3 (monkey 2).—Photograph taken twelve weeks after multiple intradermal inoculations. The inguinal nodes are enlarged, and there are large granulomatous lesions in each axillary region.

color, and the surface appeared to be somewhat granular owing to the presence of small, closely packed nodules which varied from 1 to 5 mm. in diameter. The substance was for the most part consolidated and failed to collapse when sectioned. In cut surfaces these miliary and conglomerate nodules were seen to be infiltrating most of the tissue of the lung, only a small portion of the lower lobe on either side containing air. Pus in considerable quantity poured forth from the bronchioles. Numerous similar, grayish-white nodules were present in the liver and spleen. The heart, adrenals, pancreas, gastro-intestinal tract and kidneys showed nothing of particular interest. All the lesions were proved microscopically to be caused by the fungus.

Monkey 2.—This animal was inoculated intradermally at seven sites on the abdomen with a broth suspension of the yeastlike forms following a single filling of the syringe. Although the volume of suspension injected at each site was the same (0.05 cc.), the number of organisms introduced at each site was variable, as uniform suspensions of the fungous cells cannot be maintained without constant

agitation. The culture used for these injections was obtained from the lesions of the first monkey approximately two months after that animal was inoculated.

As in the case of the first monkey, small, brownish areas of induration appeared at the sites of injection. Development of the lesions in this monkey, however, was more rapid, possibly indicating an increase in virulence of the fungus due to its passage through the first monkey. Two weeks following the injection firm nodules about 0.75 cm. in diameter were present at two of the sites. During the next week similar nodules were apparent at the other sites. All of these lesions

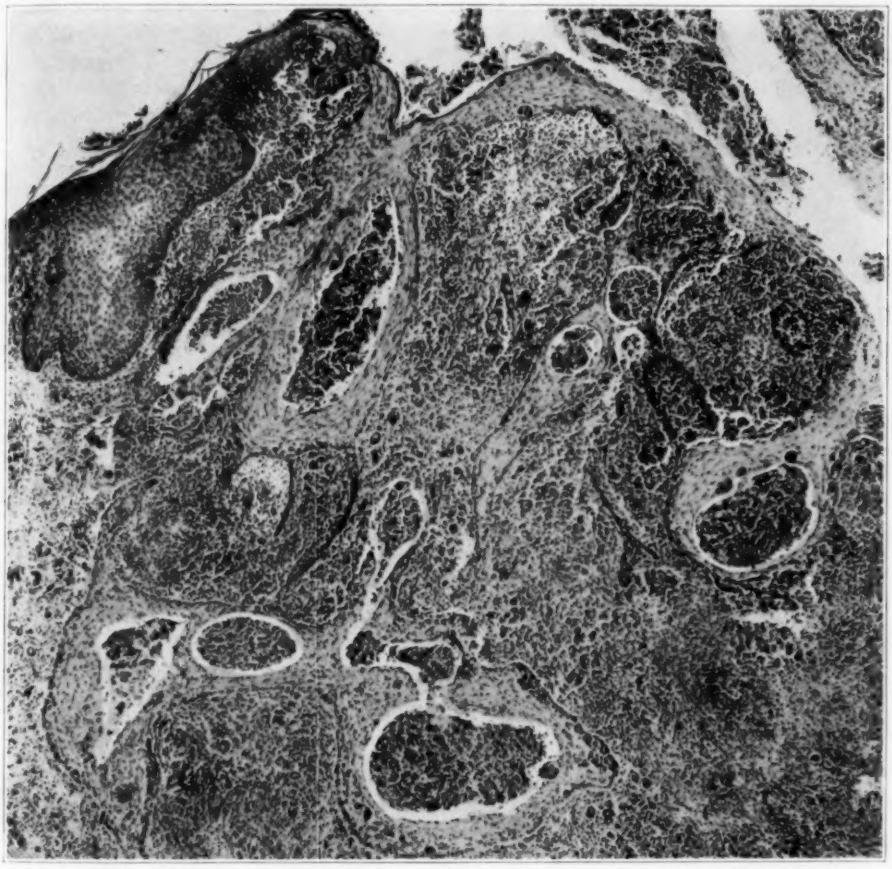

Fig. 4 (monkey 2).—A section of a chronic cutaneous lesion. Note the epithelial hyperplasia and the characteristic abscesses in the epithelium. Histologically the lesion is indistinguishable from those of cutaneous blastomycosis in man. Hematoxylin and eosin stain; × 10.

soon became ulcerated, but they remained localized for a period of approximately three months. Then, as in the first monkey, the infection spread to the superficial inguinal nodes on each side. The latter became enlarged and fluctuant, finally ulcerating to discharge large quantities of pus containing the yeastlike forms in great numbers.

Next, large granulomatous lesions developed in both axillary regions. These, too, soon ulcerated. At the same time numerous superficial ulcers appeared in the skin of the abdomen and chest. During their existence the cutaneous lesions were for the most part progressive. During the later stages of the disease, however, some of the more superficial ulcers became partially covered by thin, scaly epithelium, a feature often seen in the cutaneous lesions of blastomycosis in man.

At the end of the sixth month the animal became emaciated. Shortly thereafter the cornea of the right eye became ulcerated, with total loss of vision in that eye. As in the first monkey, there developed a hacking cough. It was killed while in a moribund condition about seven and one-half months after the inoculations were made.

Autopsy revealed numerous visceral lesions. Each lung contained miliary and conglomerate lesions like those of the first monkey, but on the whole they appeared more discrete. The lymph nodes, spleen and kidneys also contained abscesses and tubercles. In the liver there were several large abscesses. One contained about 10 cc. of pus. The entire posterior chamber of the right eye was filled with pus

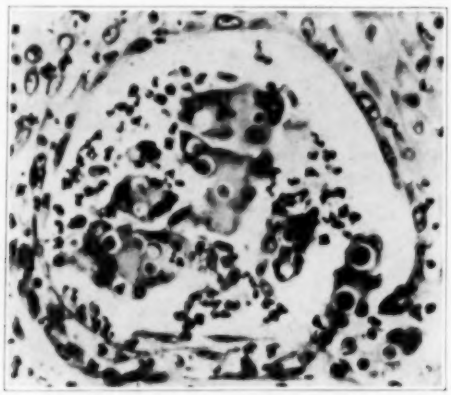

Fig. 5 (monkey 2).—A higher magnification of one of the epithelial abscesses shown in figure 4. Note the polymorphonuclear leukocytes and giant cells, with the latter containing many fungous cells. Hematoxylin and eosin stain; × 300.

which displaced the lens and caused practically complete destruction of the retina. The gastro-intestinal tract showed nothing of interest.

Portions of the cutaneous lesions removed from time to time during the course of the disease and tissues obtained at autopsy were fixed in Schaudinn's fluid [17] and stained with hematoxylin and eosin for histologic study. The earliest cutaneous lesion studied was twenty days old—induced by intradermal inoculation. The outstanding feature was the presence of numerous small epithelial abscesses which contained large numbers of polymorphonuclear leukocytes and mononuclear cells. The mononuclear cells, which were actively phagocytic, were seen to contain large numbers of small, somewhat spherical structures which proved to be fragments of nuclei of polymorphonuclear leukocytes. A few giant cells, indistinguishable from Langhans' cells, as well as epithelioid cells were present in the abscesses.

17. The formula for Schaudinn's fluid is: Saturated mercuric chloride in physiologic solution of sodium chloride, 65 cc.; alcohol, 95 per cent, 33 cc., and glacial acetic acid, 2 cc.

The yeastlike fungous cells were abundant, some lying free in the exudate while others occurred within giant cells. Within the epithelium near the periphery of the lesions were several small groups of degenerating epithelial cells, usually in association with a few polymorphonuclear leukocytes and one or more fungous cells, indicating the formation of new abscesses.

As the lesions became more chronic they were indistinguishable from those of cutaneous blastomycosis in man. The characteristic intradermal abscesses persisted. The mononuclear phagocytic cells which were so abundant in lesions in the early stage disappeared, and giant cells and epithelioid cells became more numerous. The fungous cells continued to be present in abundance. Hypertrophy of the bordering epithelium and neighboring sebaceous glands was present to a varying degree. In the tissues immediately surrounding the lesions, which were confined entirely to the skin, there was a diffuse infiltration by plasma cells and lymphocytes.

The chief lesions seen in the various internal organs were miliary and conglomerate structures that in many ways resembled tubercles produced by Koch's bacillus

Fig. 6 (monkey 2).—Large multiple abscesses in the liver.

and were both proliferative and exudative. Many were fairly well circumscribed and possessed the architecture of the ordinary tubercle, but the presence of fungous cells served to differentiate them from the ordinary tubercle. Where the exudative reaction predominated the lesions appeared as small abscesses. They then appeared as masses of polymorphonuclear leukocytes bordered by a zone of giant cells and epithelioid cells and a varying amount of fibrous tissue. Caseation, though present in some of the lesions, was not a conspicuous feature as it is in exudative lesions of tuberculosis. Some of the lesions in the lungs showed evidence of healing as indicated by masses of hyalinized connective tissue containing a few giant cells and epithelioid cells. In areas where exudative lesions were numerous the bronchioles were filled with polymorphonuclear leukocytes, giant cells and fungous cells.

The large abscesses in the liver of the second monkey possessed walls of giant cells and epithelioid cells which enclosed a mass of polymorphonuclear leukocytes, mononuclear phagocytic cells and fungous cells, all in various stages of degeneration. The abscess in the right eye of the same monkey contained a similar exudate. The retina was entirely destroyed, and giant cells, epithelioid cells and fungous cells were present in large numbers in the choroid. The conjunctiva was infiltrated

by plasma cells, polymorphonuclear leukocytes and fungous cells. Sections of the brain of the first monkey showed in the pia an exudate consisting of polymorphonuclear leukocytes and mononuclear cells but no fungous cells. The inflammatory process extended to the underlying brain tissue, as these inflammatory cells also occurred about some of the blood vessels of the cortex. Sections of bone marrow taken from a femur of each of the monkeys showed a considerable increase in the number of premature cells of the granular series but nothing else of interest.

The fungous cells occurred as spherical yeastlike forms without associated mycelium. They varied greatly in size, ranging from 3 to 24 microns in diameter, with an average of 10 microns. Both small and large forms commonly occurred

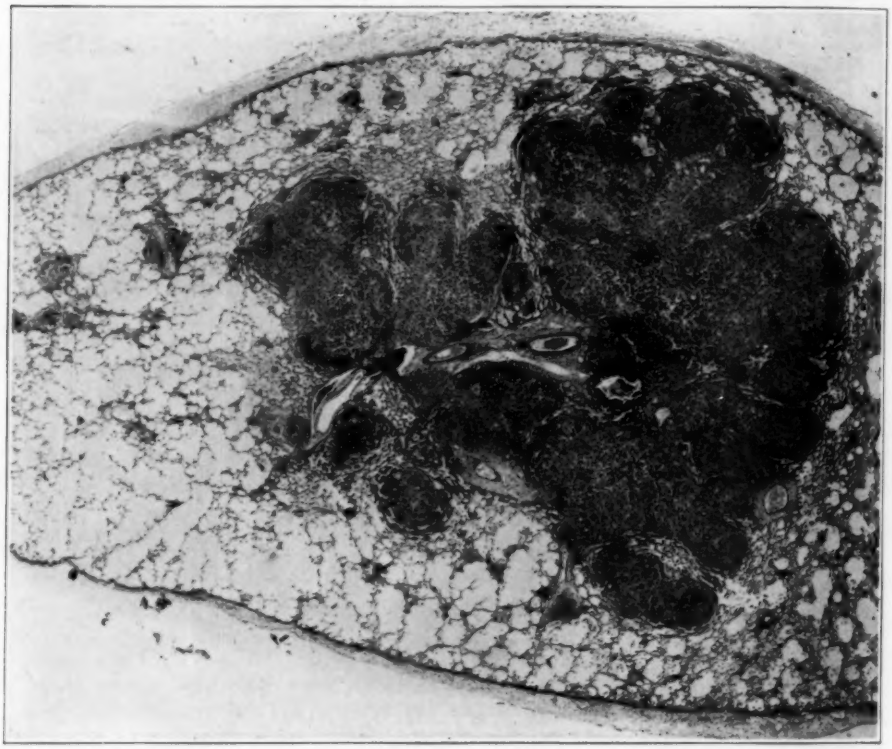

Fig. 7 (monkey 2).—A section showing miliary and conglomerate tubercles in the lung. Hematoxylin and eosin stain; × 10.

within giant cells, sometimes as many as ten or more being seen in a single cell. The great majority possessed a well defined membrane, a well marked double contour and a granular cytoplasm. Budding forms were common. In sections stained with hematoxylin and eosin the capsule remained unstained. The cytoplasm appeared as a contracted violet or pink, spherical or pyriform mass that was separated from the capsule by a clear zone. In some instances buds on the cytoplasmic masses extended outward into the clear zone without penetrating or distorting the capsule. The cytoplasm sometimes stained uniformly, but more often it was seen to contain several darkly staining granules that resembled cocci. The significance of these granules is not known. In addition to the capsulated forms

which were present in such abundance, there were seen, especially in preparations from the cutaneous lesions, numerous small forms from 3 to 5 microns in diameter with a very delicate membrane and faintly staining cytoplasm. Wade [18] described delicate fungous forms similar to these in association with larger capsulated forms in a lesion of cutaneous blastomycosis of man. Fungous cells that appeared as empty capsules and which were undoubtedly dead, were frequently seen within giant cells. Dead forms of the fungus were also common in the necrotic cellular débris of the abscesses; they were seen best in fresh preparations, in which they appeared as empty, more or less collapsed shells. I have not observed the formation of asci. Evidently the fungus proliferated in the tissues solely by budding.

MONKEY 3.—Cutaneous blastomycosis was induced by the subcutaneous inoculation of the mycelial form of the fungus. The inoculum, consisting of four small fragments obtained from a three week old dextrose agar culture, was introduced into the subcutaneous tissues of the lower portion of the abdomen by means of a

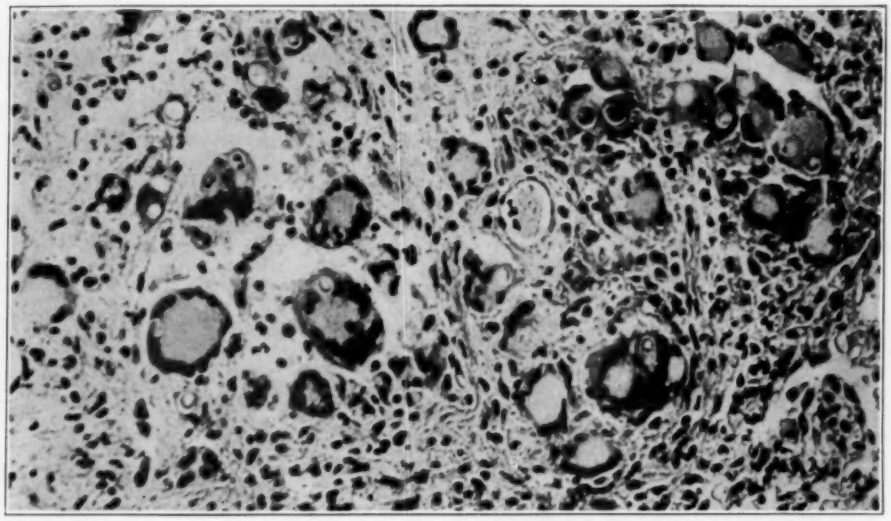

Fig. 8 (monkey 2).—A portion of a proliferative lesion which occurred in the lung. Note the numerous giant cells of the Langhans type, in many of which the fungous cells may be seen. Hematoxylin and eosin stain; × 350.

trochar. Within forty-eight hours there began to discharge through the sinus tract made by the trochar a sanguinopurulent exudate which contained yeastlike forms in great abundance. A small nodule formed in the subcutaneous tissues at the site of injection, and at the end of a week an elevated ulcer appeared about the sinus opening. At the end of the second week the superficial inguinal nodes appeared enlarged and fluctuant. The animal scratched its skin almost constantly, which probably accounts for the additional lesions which subsequently developed on the abdomen and chest. These were numerous, somewhat verrucous and granulomatous lesions from which exuded blood and pus. They soon became conglomerate, and at the time of writing this article they appear as a single lesion extending from the scrotum to the neck. The general health of the animal is still good.

18. Wade, H. W.: A Variation of Gemmation of Blastomyces Dermatitidis in the Tissue Lesion, J. Infect. Dis. **18**:618, 1916.

PATHOGENICITY OF THE FUNGUS FOR OTHER ANIMALS

Attempts have been made to induce the disease in other animals used in the laboratory, including dogs, mice, white rats, rabbits and guinea-pigs, but only in the monkey have I succeeded in reproducing lesions similar to those of cutaneous blastomycosis of man.

By means of subcutaneous injection of cultures of the mycelial form, ulcerative lesions have been induced in five dogs. These lesions, which developed immediately following the injection, appeared as flat masses of weeping granulation tissue that projected slightly above the level of the surrounding skin. The surface was covered by a purulent exudate that contained, in addition to many spherical fungous cells like those seen in the lesions of the monkey, many elongated fungous cells, often in chain formation. Epithelial hypertrophy, one of the characteristics of the lesions of the monkeys, did not occur. Similar lesions were induced in these animals by means of intradermal and subcutaneous injection of cultures of the

Fig. 9 (monkey 3).—Lesions induced by a single subcutaneous inoculation of the mycelial form of the fungus in the lower portion of the abdomen near the midline sixty-two days before the photograph was taken. Note the similarity of the lesions to the verrucous lesions on the patient's cheek.

yeastlike form of the fungus. Although some of these ulcers reached a size 4 or 5 cm. in diameter and in some cases the superficial inguinal nodes became involved in the infectious process, all healed in from four to eight weeks following the inoculation. The process of healing, once initiated, took place rapidly.

Mice proved somewhat variable in their response to intraperitoneal injections of the mycelial form of the fungus. During the course of the experiments in which such animals were employed for obtaining cultures of the yeastlike form of the fungus, at least three dozen received intraperitoneal injections of mycelium. Since not more than half of them were killed for the cultural experiments, the remainder were observed for evidence of generalized infection, some for as long as four months. Only three died, and in each the lungs, liver and spleen showed abscesses containing many yeastlike cells. However, the results following similar injections of yeastlike forms were more constant: Each of six mice died in from three to five weeks after inoculation, and numerous small abscesses containing the fungous cells were found in the lungs, liver, spleen and kidneys.

In rats, rabbits and guinea-pigs intradermal and subcutaneous injections of cultures of the yeastlike form produced only localized abscesses which healed completely in from three to six weeks. Similar results were obtained in these animals following subcutaneous injections of cultures of the mycelial form.

CULTURES FROM EXPERIMENTAL LESIONS

From time to time the fungus was cultivated from the lesions of the monkeys. Material from lesions a few weeks old yielded colonies of both forms of the fungus on rabbit blood agar after three days of incubation at 37 C. On dextrose agar, cultures obtained from either acute or chronic lesions yielded only a mycelial growth. As the lesions became more chronic it became increasingly difficult to regain the fungus in culture, even if contaminating bacteria were not present.

The retardation of growth of the fungus derived from chronic lesions on artificial culture mediums is probably due to a substance or substances of the nature of an antibody, and its effect is reduced by dilution. In making cultures from chronic lesions it has been my experience that better and more rapid growth is obtained if the material to be cultured is first extracted with a considerable volume of broth in the icebox for a period of from one to two weeks before being planted on a solid medium.

Since the lesions of cutaneous blastomycosis are usually contaminated with staphylococci or other bacteria that retard or prevent the growth of the fungus in primary cultures, the well known antiformin method applicable to tuberculous material was employed. Neither the fungus nor contaminating bacteria grew in cultures of the treated material.

IMMUNOLOGIC REACTIONS

Immunologic studies in blastomycosis up to the present time have yielded only conflicting results. The presence of agglutinins, precipitins and positive complement-fixation reactions have been reported by some investigators but denied by others. Judging from preliminary observations that I have made on animals used for experiments, I believe that a variable degree of immunity is established to the infection. One of the dogs in which a granulomatous lesion was induced by a subcutaneous injection of the fungus was reinoculated about two weeks after the initial lesion had healed. An abscess developed immediately at the site of the second injection and ruptured on the second day. On the following day smears from the abscess failed to reveal any fungus forms. On the eighth day following the second injection the abscess was completely healed, whereas the initial injection had resulted in a granulomatous lesion in which fungous cells could be demonstrated for at least six weeks. When the serum of this animal was tested against the yeastlike form of the fungus no agglutinins or precipitins

were demonstrated. Indeed, the fungus grew in the serum apparently as well as in normal serum.

Two of the monkeys with experimental lesions of about three months' duration were also reinoculated subcutaneously. Abscesses developed at the new sites but disappeared within one week. No change, however, could be detected in the nearby, preexisting lesions. Such an immune reaction as this appears to be may explain the relative infrequency of secondary lesions due to auto-inoculation in cases of chronic cutaneous blastomycosis in man. In both man and monkey, however, when this immunity is broken down the infection tends to become systemic.

COMMENT

Recent investigations have shown that cutaneous and systemic blastomycosis may be due to a variety of fungi which are indistinguishable in the lesions. All of these species occur in the lesions which they produce as large, round to oval cells having a well defined membrane, a well marked double contour and a granular cytoplasm. They multiply in the tissues by budding. Since the tissue forms of these species are indistinguishable from each other, cultural studies are necessary for their differentiation.

The fungus responsible for the case of cutaneous blastomycosis reported in this paper proved to be identical with M. tulanense Castellani. It is noteworthy that the lesions from which my strain was obtained responded readily to potassium iodide therapy.

This species grows well on the various mediums generally employed for the cultivation of fungi, but only in the mycelial form, usually producing conidia and chlamydospores in abundance. When cultures of such mycelial forms are introduced into the tissues of a susceptible animal the mycelium breaks up to form elongated cells with rounded ends. The latter rapidly become spherical, acquire a thick membrane and in every particular assume the appearance of the yeastlike cells seen in lesions of blastomycosis of man. The conidia and chlamydospores injected likewise rapidly assume a similar appearance and begin to proliferate by budding, indicating their close relationship to the yeastlike or tissue form of the fungus.

When obtained from early experimental lesions the fungus tends to proliferate in the yeastlike form on mediums rich in protein, provided the temperature of incubation is approximately 37 C., rather than to produce mycelium, as do similar forms derived from chronic lesions and cultivated under similar conditions. Most of the fungous cells in young blood agar cultures possess thin membranes. As these cultures grow older, however, more and more of the cells acquire thick capsules, and finally, when growth ceases, practically all have thick capsules and

appear indistinguishable from the fungous cells in lesions. Such an evolution indicates that the final form assumed by the yeastlike cell in blood agar cultures is the chlamydospore, which corresponds to the form of the fungus seen in lesions. The buds formed by these cells in either lesions or cultures represent the anlagen of mycelia, which, owing to conditions of unfavorable environment, are unable to form hyphae but instead develop into other chlamydospores.

Comparison of this fungus with one of the original strains of M. tulanense sent to me from London by Sir Aldo Castellani has convinced me that the two fungi are identical. The original strain grows on blood agar, and its yeastlike form has been readily obtained on this medium after rapid passage of its mycelial form through mice.

I have succeeded in inducing in monkeys chronic cutaneous lesions which are typical of the lesions of cutaneous blastomycosis in man. The disease pursued a chronic course, finally terminating in a fatal systemic infection. The chief lesions found in the internal organs, like those of systemic blastomycosis in man, were miliary and conglomerate structures which were similar to the well known tubercles produced by Koch's bacillus.

Only in the monkey have I succeeded in reproducing lesions similar to those of cutaneous blastomycosis in man. Subcutaneous and intradermal inoculations of either form of the fungus produced in rats, rabbits and guinea-pigs only localized abscesses which soon healed. Similar inoculations in dogs resulted in weeping, granulomatous ulcers which healed in the course of from four to six weeks. Mice have proved somewhat more susceptible to infection by the fungus. When these animals were inoculated intraperitoneally with cultures of the yeastlike form rapidily fatal, systemic infections developed, resulting in numerous abscesses in the lungs, liver, spleen and kidneys.

Recently I have isolated another fungus from the lesions of systemic blastomycosis. Although not definitely identified as yet, the studies thus far indicate that it is not M. tulanense. The yeastlike form of this species has also been obtained on culture mediums after rapid passage of its mycelial form through mice. Also, cutaneous lesions have been induced in a monkey by intradermal injections. Although this animal was inoculated only five weeks ago, the course of the lesions up to the time of writing indicates that they will become chronic and that their subsequent course will be similar to that of the lesions induced in the other monkeys by the injection of cultures of M. tulanense.

Since two species capable of causing blastomycosis have induced in monkeys lesions typical of cutaneous blastomycosis in man, all of the fungi in this category may prove capable of inducing similar lesions in these animals.

Identification of the responsible fungi in a considerable number of cases of blastomycosis may serve to correlate the different fungi with the types of lesions which they produce and may perhaps be of assistance in determining the prognosis in individual cases of the disease. The reproduction in monkeys of the chronic form of the disease which shows no tendency to heal spontaneously affords an opportunity for experimental therapy not heretofore practical in animals with either abortive lesions or rapidly fatal generalized infections.

Preliminary observations that I have made on experimental animals indicate that a variable degree of immunity is established to this infection. Further studies, however, are required to determine the nature and significance of this immunity.

SUMMARY

A case of cutaneous blastomycosis of nine years' duration is reported.

The etiologic agent proved to be M. tulanense Castellani.

This fungus may be cultivated either in the yeastlike form as it occurs in the lesions or as a mycelium.

Lesions typical of cutaneous blastomycosis in man have been induced in three monkeys by means of subcutaneous and intradermal injections of cultures of the fungus.

As in man, the experimental disease in monkeys tends to become systemic.

The production of the disease experimentally in the skin of monkeys affords an opportunity for experimental therapeusis of cutaneous blastomycosis.

The pathogenic phase of the fungus is fundamentally a chlamydospore which germinates in tissues by building and appears as a yeastlike form.

CONGENITAL DEFECT OF THE SKIN OF THE NEW-BORN

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Descriptions of a limited number of instances of congenital defect of the skin of the new-born are to be found in the literature. Most of these have appeared in publications devoted to pediatrics. It is of interest to note a case first recognized when the patient was in his thirty-eighth year.

Congenital defect of the skin of the new-born is an extraordinary condition, characterized by absence at birth of circumscribed areas of integument. The defect is usually solitary, but lesions may be multiple, in which case they are usually either grouped or symmetrically located. The outline is sharply defined and circular or oval in most instances and from 1 to 5 or more cm. in diameter. The epidermis and dermis are absent, but the subcutaneous tissue is little affected, and there is no evidence of inflammation. The site of predilection is the vertex of the scalp, but cases have been described in which the integumentary loss involved a large area of each side of the trunk (Hahn [1]), and in Abt's case [2] the loss of skin occurred on the anterior aspect of both knees.

Biopsies made immediately after birth have shown no inflammatory infiltration and a complete absence of epidermal structures.

No relation of the incidence of the anomaly with trauma during parturition has been noted. To hypothesize that amniotic bands are responsible would not account for the symmetry of the multiple lesions, and no direct evidence of adherence to membranes has been demonstrated.

I am inclined to believe that the defect originates in early embryologic periods as a discontinuity due to tension during expansion of the area of presumptive epidermis in the gastrula stage.[3]

The usual clinical course is granulation and uneventful healing of the defect, the cicatricial tissue, however, being permanently without epidermal accessory structures.

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1. Hahn, W. T.: Angeborner Defect eines grossen Theils der Haut des Rumpfes, J. d. Chir. u. Augenh. **30**:156, 1841.

2. Abt, I. A.: Congenital Skin Defects, Am. J. Dis. Child. **14**:113 (Aug.) 1917.

3. Huxley, J. S., and DeBeer, G. R.: The Elements of Experimental Embryology, London, Cambridge University Press, 1934, p. 25.

REPORT OF CASE

W. G. B., a white man aged 38, an automobile mechanic, came to my office on Sept. 26, 1934. He said that he has a twin brother who does not resemble him physically. He said that he was a "7 month baby" and that the period of delivery, so far as his mother was concerned, was uneventful and no instruments were used. Shortly before his birth a child in the community had been severely burned; the raw, scalded surfaces had astonished and terrified his mother, and when he was born the raw surfaces of the sides of his body were at once attributed to

Congenital defect of the skin healed for about thirty-eight years. The lesions were symmetrical on the sides of the trunk, as in Hahn's [1] case.

this prenatal influence. He had no other explanation of his unusual birth mark. The twin was normal.

The lesions may better be understood from illustration than from description. Symmetrically located on the lateral aspects of the trunk, they were manifested as large cicatrices, closely resembling the scars of old burns. The tissues were soft and pliable, of normal color, with no pigmentation, no keloid formation, and little telangiectasis. A few winding subepidermal capillaries were visible in the seamlike cords where the wounds had knit. These cords branched in three directions from a common meeting point in the midaxillary line overlying the eighth rib. One branch extended to the inferior angle of the scapula, one toward the

free end of the twelfth rib and one toward the umbilicus. In the areas involved, sensation was normal, and the state of nourishment of the tissues was good, but no hairs were present. There were no subjective symptoms.

No other integumentary anomaly was observed.

No diagnosis other than congenital defect of the skin of the new-born is tenable.

SUMMARY AND CONCLUSIONS

A case of congenital defect of the skin of the new-born is described as observed long healed in adult life. This rare form of birth mark is thought to be due to disturbance of the expansion of the area of presumptive epidermis in early embryologic life. These anomalies are to be differentiated, when met in the adult, from the scars of old burns. The diagnosis depends on the history of defect of the skin present at birth and, objectively, on the location of the resultant cicatricial tissue, which supports no epidermal accessory structures.

1308 Bryant Building.

NONULCERATIVE TUBERCULOSIS OF THE MOUTH FOLLOWING DENTAL PROCEDURE

REPORT OF A CASE

CHARLES ROBERT REIN, M.D.

AND

M. HILLEL FELDMAN, D.D.S.

NEW YORK

Recently, we observed a patient in whom an unusual form of nonulcerative tuberculosis developed in the soft tissues of the mouth following a regular dental procedure.

REPORT OF CASE

Mrs. A. J., an American, aged 27, a housemaid, visited her dentist on Aug. 12, 1933, because she had chipped the upper left cuspid. Owing to the severe pain when the drill was applied, the dentist devitalized the tooth under local anesthesia on September 6. A solution prepared by dissolving a tablet of procaine hydrochloride (E tablet) in Ringer's solution was injected infra-orbitally to produce local anesthesia. The root canal was treated and filled with gutta-percha dissolved in chloroform. Three weeks later the inlay was introduced. During this procedure the patient stated that she felt a burning pain over the area of the cuspid. Two hours later she first noticed a small hard mass in the soft tissues of the left cheek immediately below the medial half of the zygoma. The following day she returned to the dentist, who advised the use of warm wet dressings. The mass continued to increase in size, and on October 11 the treated cuspid was extracted under infra-orbital anesthesia similar to that used in devitalization. After extraction the mass continued to increase in size. On November 6 the patient was sent to one of us (M. H. F.) for excision of the growth through a mucobuccal incision, which was performed under general anesthesia. Following the operation a marked swelling of the entire left cheek developed. This swelling subsided in a week, but the patient noticed that the mass had already recurred. On November 20 the upper left bicuspid was extracted under general anesthesia, and the recurrent mass was again removed. The tissue was sent to the laboratory for microscopic examination.

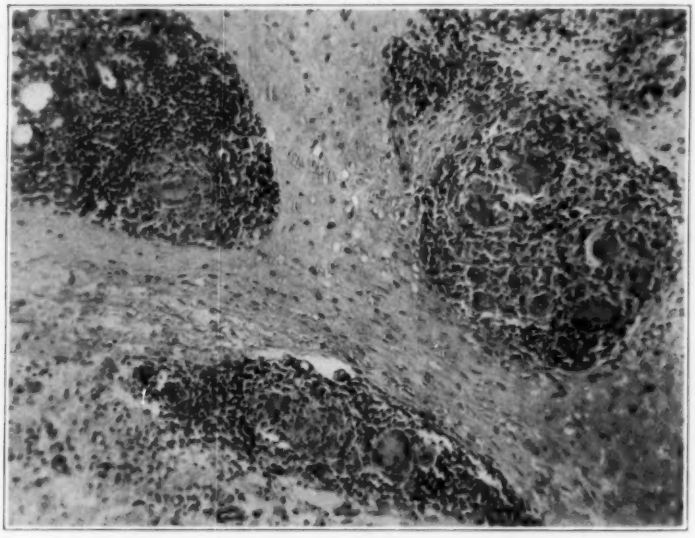
Physical examination revealed a well developed and well nourished, slightly obese woman. The general examination revealed nothing abnormal except for the presence of a firm subcutaneous tumor, the size of a hickory-nut, which seemed to be attached to the inferior border of the zygoma of the left cheek. The mass was slightly painful on palpation. The skin and oral mucosa of the left cheek were normal except for the incision in the upper mucobuccal fold on the left side, which appeared to be healing well.

Histologic examination (Dr. Satenstein) revealed that in the middle and deep layers of the cutis there were numerous discrete and confluent tubercles. Throughout the entire cutis there were numerous small, thin-walled blood vessels and a cellular infiltration containing connective tissue cells, plasma cells, fibroblasts and occasional giant cells.

The diagnosis was tuberculosis cutis (tubercles, inflammatory process and granulation tissue). The slides were also seen by several other pathologists, who expressed the belief that the tissue was either definitely tuberculous or highly suggestive of tuberculosis.

On December 15 (twenty-five days after the second mass had been removed) another recurrent mass was removed for animal inoculation and microscopic examination. The microscopic picture was similar to that seen in the previous examination.

Juices were expressed from part of the tissue in a tissue press and suspended in a solution of sodium chloride. This suspension was injected subcutaneously into a guinea-pig. The first pig to be inoculated died in eight days. On December 23 a second pig was inoculated with the remainder of the solution, which had been kept in the refrigerator. The second pig showed no loss in weight, and there was



Section of the cutis showing formation of tubercles, cellular infiltration and granulation tissue.

no enlargement of the inguinal lymph nodes. Koch's tuberculin, injected subcutaneously on Jan. 20, 1934, produced no reaction. The reactions of the guinea-pig remained negative until March 26, 1934.

Patch tests were performed on the patient with Koch's tuberculin (undiluted), which gave strongly positive eczematous reactions. Reactions to the tuberculin were positive in dilutions of 1 : 100,000 and 1 : 1,000,000.

Roentgen examinations of the lungs revealed old central tuberculous foci of the puerile type, old Gohne nodes and moderate secondary bronchial thickening of the root and branches. Roentgenograms of the mouth revealed a small, opaque foreign body the size of a pinhead in the area of the upper left cuspid. This was probably gutta-percha which had been forced through the root canal during treatment. Roentgenograms of the sinuses showed nothing abnormal.

Complete blood counts and differential counts were normal. The Wassermann and Kline reactions were negative. Repeated urinalyses gave negative results.

The patient received several injections of neoarsphenamine and a bismuth preparation with no effect. She then received several generalized exposures to ultraviolet radiation, followed by five exposures of the lesion to roentgen rays (1 skin unit through a 3 mm. aluminum filter) at intervals of six weeks. After the fifth exposure, the entire lesion disappeared.

COMMENT

This case presents several unusual points of interest. Since the granuloma developed so close to the infra-orbital area, it is possible that infra-orbital injection of the anesthetic produced a *locus minoris resistentiae* in which a secondary tuberculous process might develop. One pathologist who examined the slides thought that tuberculosis had developed in an accessory lymph node. It is also possible that an oily solution of the anesthetic may have been accidentally injected, producing a paraffinoma, oleoma or vaselinoma. At times tumors induced by oil may show a pronounced tuberculoid structure, the texture of which, however, differs from that seen in this patient. Although the actual fatty substances may have been absent from this section, hollow spaces or depressions which previously contained the oily material should have appeared. The tuberculoid process which usually develops around these small spaces did not occur in this case. It is difficult to rule out the possibility of a foreign body reaction resulting from the presence of the small amount of gutta-percha which was demonstrated by the roentgenogram in the soft tissue in the area of the cuspid. Another possibility is that the infection was introduced into the tissues with the needle or drug at the time of the infra-orbital injection.

One pathologist suggested that the tumor was a neuroma which had developed at the amputated end of the dental nerve following devitalization of the tooth.

There are three factors which seem to point against a tuberculous process: (1) the negative results of animal inoculation, although it is questionable whether the suspension of tissue juices in the solution of sodium chloride which was prepared on December 15, was still suitable for the inoculation of the second animal after an interval of eight days; (2) inability to demonstrate tubercle bacilli in the tissue, and (3) the usual association of tuberculosis of the mouth with pronounced pulmonary symptoms. However, a number of patients with tuberculosis of the mouth have been observed in whom the pulmonary symptoms were slight.

CONCLUSIONS

We have here described a case which is believed to be a nonulcerative form of tuberculosis, the development of which was favored by dental intervention.

A NEW SYPHILITIC DENTAL DYSTROPHY (SIMILAR TO THE BUD MOLAR OF PFLÜGER)

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BOSTON

I wish to report on a type of dystrophy of the 6 year molars which I have observed in a number of cases of congenital syphilis.

In cases of dystrophy of this sort the diameter of the crown is normal, and there is no deficiency of enamel or special tendency to early caries. The cusps, of normal size, are rolled inward without any shoulder at the crown and give the appearance of being clinched.

The impression for figure 1 was taken from the tooth of an underdeveloped girl aged 9 years who also showed Hutchinson teeth and a suggestive facies. The Hinton test was positive.

I have observed these changes only in cases of congenital syphilis, though it is probable, as is true of cases of the typical mulberry molar, that they may occasionally be found in cases of nonsyphilitic conditions due to some long illness occurring in the first year.

In contrast, the so-called mulberry molar first described by Fournier showed a marked tendency to early caries of the occlusal surface. If it is seen soon after eruption, it shows a broad crown of normal enamel surmounted by poorly developed cusps which have fairly good enamel and are clumped together. The remaining portion of the occlusal surface is undersized, discolored and rough, with a distinct shoulder where the cusps join the crown.

Of interest in connection with the development of such teeth in the embryo is Karnosh's [1] study of congenital syphilitic teeth. In an excellent histologic study on syphilitic hypoplasia of the teeth he found that only a minute portion of the first permanent molar is actually formed in utero, that calcification of the enamel begins about one month before birth and that such a deposit is limited to three or four isolated caps or spicules. The bulk of the occlusal surface is laid down during the first year; the cusps do not attain their full size until well into the second year, and calcium deficiencies occurring at this time are likely to produce the greatest degree of distortion. Karnosh's [1] conclusions are that the teeth-forming organs are not seriously impaired in utero and

1. Karnosh, L.: Histopathology of Syphilitic Hypoplasia of the Teeth, Arch. Dermat. & Syph. **13**:24 (Jan.) 1926.

that most of the deciduous teeth as well as the prenatal caps of the first permanent molars are fairly well formed in spite of the presence of active syphilis in the fetus.

Fig. 1.—Photograph of an impression of a tooth with dystrophy in an underdeveloped girl, aged 9.

Fig. 2.—Photograph of an impression of a mulberry molar.

Since preparing this paper, an abstract of an article in *Venereal Disease Information* for June 1934 mentioned the bud molars described by Pflüger. The description and photographs in the original article,[2]

2. Schwisow, W.: Congenital Syphilis and the Teeth, Dermat. Wchnschr. **98**:101 (Jan. 27) 1934.

as well as a description by the same author in collaboration with Kreyenberg,[3] lead me to believe that the bud molar of Pflüger and the tooth which I have described, which I formerly considered to be an original observation, are the same.

However, since the specific defect is not generally recognized, in this country at least, it seems worth while to call it to the attention of the medical profession.

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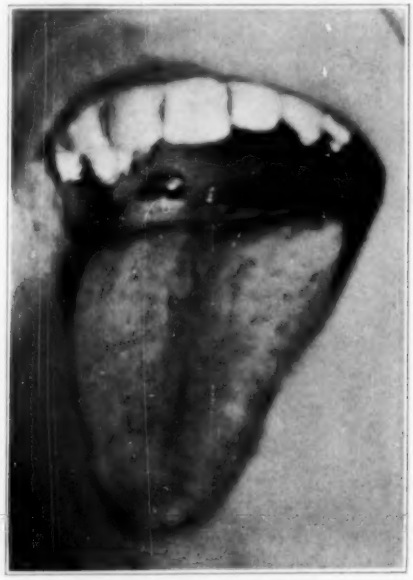
3. Kreyenberg, G., and Schwisow, W.: Die Beziehungen des "Hutchinson-Zahnes" und des "Pflügerschen Knospenmolaren" zur kongenitalen Syphilis, Ztschr. f. d. ges. Neurol. u. Psychiat. **127**:188, 1930.

Minor Notes

GRANULOMA PYOGENICUM OF THE TONGUE

RICHARD J. KELLY, M.D., NEW YORK

The unusual feature about the case of granuloma pyogenicum reported here is the location of the lesion. Several authors, among them R. L. Sutton Sr.[1] and R. L. Sutton Jr.,[2] have reported cases in which there were lesions on the lips, the tip of the tongue and the gingivae, but a careful search of the literature reveals no mention of the occurrence of the lesion on the posterior third of the tongue.



Granuloma pyogenicum of the posterior third of the tongue.

F. C.,a white girl aged 13, was seen about ten days after the appearance of the lesion. Her first symptom was slight irritation with roughness on the right side of the tongue posteriorly. Three days later she noticed an elevated mass the size of a pinhead over one of the circumvallate papillae. This mass increased in size during the next ten days, until at the time of examination it was the size of a large pea. There was at this time slight tenderness of the tongue and a sense of annoyance on swallowing.

1. Sutton, R. L., Sr.: Granuloma Pyogenicum of the Lip, J. A. M. A. **66:** 1613 (May 20) 1916.

2. Sutton, R. L., Jr.: A Fissured Granulomatous Lesion of the Upper Labio-Alveolar Fold, Arch. Dermat. & Syph. **26:**425 (Sept.) 1932.

The lesion had the typical reddish-gray appearance of granuloma pyogenicum. It was slightly compressible, ending in a raised, annular and firm base (the hernia ring formation often seen with granuloma pyogenicum). No submental adenopathy was apparent. The history gave no information indicating that the affected area was traumatized at any time. However, the right upper molars were pointed and somewhat roughened on their medial borders, thus offering a possible clue to the source of irritation.

Because of the typical appearance of the lesion and also because of its location, biopsy was not performed.

The lesion was removed by electrocoagulation and curettement under anesthesia with procaine hydrochloride.

140 East Fifty-Fourth Street.

USE OF ADRENAL SUBSTANCE IN CASES OF DERMATOSES WHICH MAY HAVE A MENSTRUAL FACTOR

WILLIAM ALLEN PUSEY, M.D., AND HERBERT RATTNER, M.D., CHICAGO

For some years we have been prescribing adrenal substance for girls with acne when they complain of minor menstrual disturbances or when with each menstrual period there is a noticeable flare-up of acne lesions. We are uncertain of its value for the relief of acne, but we have had some interesting experiences. It is not uncommon to have the patients report later, gratefully, relief from menstrual cramps, more regular flow and improvement in the general well-being. They are given 2 grains (0.13 Gm.) of desiccated whole gland substance three times daily by mouth. There is, of course, considerable experimental evidence available to indicate that the adrenal cortex has a decided influence on the gonads, particularly in the female. There is evidence also of cortical influence, so that the use of adrenal substance for menstrual abnormalities has some basis. We are aware that endocrinologists generally deprecate the use of glandular substances, other than thyroid, when given by mouth, but the beneficial results are sometimes so striking as to preclude doubt.

About two years ago a woman aged 28, married, with one child, on presenting herself had a symmetrical eruption on the face which we considered to be discoid lupus erythematosus. It had been present at intervals for one and one-half years, and lesions had reappeared one month previously. Since a colleague in another city had effected good results with injections of gold sodium thiosulphate, we gave her more, and after the second injection the lesions disappeared. The next month there was a flare-up coincident with the menstrual period. After pointed questioning, it was learned that the exacerbations of the eruption usually came at the menses; that the patient always experienced severe cramps, which two operations had failed to relieve, and that there was a copious flow of blood. In all other respects she enjoyed excellent health. She was given tablets of adrenal substance to take during the menses, beginning a few days prior to the onset. After the next menstrual period she reported that for the first time since its beginning there had been no flare-up in the eruption, that the menstrual flow was scantier and that the cramps were practically negligible. We saw her again seven months later. There had been no recurrence of the eruption. It is of interest, however, that when

during one month she had neglected to take adrenal substance the menstrual disturbance returned, so severely that "nothing could ever again keep her from taking the medicine."

Our purpose here is to record the excellent result from adrenal substance in a case in which the condition was clinically diagnosed as lupus erythematosus. The clinical picture lacked many of the features that have been described as typical of dermatitis dysmenorrhoeica. The lesions were at all times dry, with a tenacious scale, and of the redness of lupus erythematosus. The outbreak was not preceded by subjective sensations, nor were there any of the later changes, vesiculation, crusting and follicular hemorrhage that are said to be a part of dermatitis dysmenorrhoeica.

7 West Madison Street.

Clinical Notes

TREATMENT OF VITILIGO WITH GOLD SODIUM THIOSULPHATE GIVEN INTRAVENOUSLY AND SUBCUTANEOUSLY

JACOB L. GRUND, M.D., BOSTON

In 1929, Lindsay [1] described the favorable results which he obtained in a case of vitiligo by means of gold sodium thiosulphate injected intravenously. With the exception of a recent communication by Burgess,[2] the relatively few subsequent reports dealing with the subject [3] indicate that the treatment is without distinct value.

The following case of vitiligo occurred in a Negro, a fact which facilitated observation of the degree of pigmentary change present as a result of gold therapy.

REPORT OF A CASE

W. R., a Negro, aged 28 years, applied for the treatment of depigmentation of the face, neck, upper part of the chest and lower part of the back, which had been present for three years. The onset dated back to a period when the patient was in the midst of intense musical study. Oil of bergamot had been applied without results. On Dec. 20, 1933, intravenous treatment with 0.05 Gm. of gold sodium thiosulphate was begun, injections being given at weekly intervals. Following the sixth injection a definite laying down of pigment was noticeable in the patches on the face and neck. There was a slight deposit also in the areas on the upper part of the chest and on the back. The pigmentation was not homogeneous and was slightly lighter than the normal skin.

On March 14, 1934, a solution of gold sodium thiosulphate was injected subcutaneously in various portions of a palm-sized leukodermic area in the infraclavicular region, an area that had been unaffected by the intravenous treatment. Five hundredths of a gram of gold sodium thiosulphate was dissolved in 2 cc. of a solution of procaine. Three or four minims of this were then injected in each of several areas. The lower third of a large area in the right supraclavicular region was similarly treated. The patient was seen again one week later. He had had a slight amount of pain and reddish edema for four days at and surrounding the points of injection. There were discernible at this time about nine pinhead-sized

From the Department of Dermatology and Syphilology, Massachusetts Memorial Hospitals and the Boston University School of Medicine.

1. Lindsay, H. C. L.: The Treatment of Vitiligo with Gold, Arch. Dermat. & Syph. **20**:22 (July) 1929.

2. Burgess, N.: Successful Treatment of Vitiligo, with Report of a Case, Brit. J. Dermat. **46**:331 (July) 1934.

3. (*a*) Maloney, in discussion on Bechet, P. B.: Leukoderma Treated with Aurotherapy Followed by Dermatitis, Arch. Dermat. & Syph. **21**:508 (March) 1930. (*b*) Pillsbury, D. M., and Kulchar, G. V.: Gold Dermatitis Limited to Depigmented Skin, Arch. Dermat. & Syph. **27**:37 (Jan.) 1933. (*c*) Becker, S. W.: Vitiligo, Arch. Dermat. & Syph. **28**:497 (Oct.) 1933.

Fig. 1.—Illustration of the filling in with new pigment of large previously leukodermic areas on the sides of the neck and face after six intravenous injections of gold sodium thiosulphate. There is also a slight laying down of pigment in an infraclavicular patch of vitiligo on the right, which had in part been infiltrated by gold sodium thiosulphate on three different occasions.

Fig. 2.—Illustration of the almost entire refilling of a palm-sized leukodermic infraclavicular patch which had been subcutaneously infiltrated by gold sodium thiosulphate on five different occasions. Filling in of new pigment is also evident at the lower third and midportions of a supraclavicular patch. The deposit of pigment corresponded to the areas into which the injections were made.

deposits of pigment in the infraclavicular patch. The supraclavicular patch presented similar changes. These regions were again treated, and the patient was seen a week later, when the first photograph (fig. 1) was taken. The newly pigmented areas had enlarged and had coalesced in places. A patch of depigmentation on the lower part of the back was entirely filled with new pigment. He received additional subcutaneous injections in the supraclavicular and infraclavicular lesions on April 25 and 30. The patient was not seen again until November 30, when the second photograph (fig. 2) was taken, which illustrates the almost entire filling of the right infraclavicular patch of leukoderma. Deposits of pigment were noticeable also in the supraclavicular patch on the right, limited to the areas of injection. To date (March 1935) the affected patches have shown diminution neither in extent nor in the degree of pigmentation produced by the treatment.

COMMENT

The laying down of new pigment in this case of vitiligo illustrates the ability of gold to affect directly the tissues involved in this condition. That the action is selective is evidenced by the fact that the normal tissues remained unchanged. It is impossible to describe the exact effect of gold therapy in vitiligo, since the physiologic action of gold on the skin is as yet unknown.[3b] Bloch's [4] studies indicate that in vitiligo the cells concerned with pigment production, namely, those with a positive dopa-oxidase reaction, enter a state of exhaustion due to the action of some undetermined stimulant or toxic agent. He expressed the belief [5] that the basal palisade cell is directly involved in the process. The recent studies of Becker and his collaborators [6] strongly suggest, however, that it is the clear cell of Masson, situated at the epidermodermal junction, which regulates pigment formation. Whichever of the preceding views is the correct one, it is logical to assume that gold, possibly through some stimulating action, affects the pigment-forming cells in vitiligo in such a manner that they again assume their normal function.

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4. Bloch, B.: Zur Pathogenese der Vitiligo, Arch. f. Dermat. u. Syph. **12:** 207, 1917.

5. Bloch, B.: Das Pigment, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 1.

6. Becker, S. W.; Praver, L. L., and Thatcher, H.: An Improved (Paraffin Section) Method for the Dopa Reaction, Arch. Dermat. & Syph. **31:**190 (Feb.) 1935.

Editorial

THE NINTH INTERNATIONAL DERMATOLOGICAL CONGRESS

The Committee of Organization of the Ninth International Dermatological Congress, to be held in Budapest, Sept. 13 to 21, 1935, under the leadership of Professor Nekam, has wisely issued a very full preliminary program. It shows several departures from the plans of previous congresses which will probably prove desirable. The greatest difference will be the time which is to be given to the consideration of the great dermatologic problems that are not purely scientific, i. e., technical, administrative and professional problems. Committees will be formed and conferences held on these nonscientific questions, and in order not to interfere with the scientific program the meetings of these committees and the conferences on general dermatologic problems will be held on September 13 and 14, preceding the opening of the scientific congress. The members of these committees are selected by the national dermatologic societies. The special committees will consist of: the permanent committee of the International Dermatological Association, a committee on the reform of dermatologic terminology, a committee on the classification of cutaneous diseases, a committee on the teaching of dermatology, a committee on the exchange of scientific and teaching material and a committee on professional problems of dermatovenereal practice.

This new feature of the congress has many attractions. It promises to bring forward much needed discussion on many of the difficulties encountered in the teaching and practice of dermatology, concerning which an international exchange of views will be valuable, and to give the congress a greatly added interest.

There will be a retrospective and a scientific exhibition, a demonstration of microscopic preparations and a comparative dermatologic exhibit for the study of cutaneous diseases which are transmissible from animal to man and from man to animal.

One afternoon will be devoted to the presentation of patients. More attention than usual will be given to features of historical interest, to the exhibition of modern scientific apparatus, to pathologic and therapeutic items and to a technical commercial exhibit.

The most radical, and it may be the most important, departure from the organization of previous congresses, which will make the congress truly an international one, is the provision that the delegates

will be designated by their national societies and thus will be representative.

Membership in the congress is open to all medical practitioners, subject to the technical requirements of the congress.

The program of the scientific deliberations of the congress consists of a large number of papers on interesting topics by able dermatologists. This program should be all that could be expected of it.

The deliberations of the scientific congress will be opened on September 15 with a social festival, the detailed program of which will be published later. It cannot be doubted that this formal opening will be impressive and attractive, as will be the other social features.

The provisions for hotels and lodgings, excursions and sight-seeing and aid in providing transportation have been carefully looked after.

The organizers of the present congress, particularly the members at Budapest, headed by Professor Nekam, who will bear the brunt of the work, have shown great foresight, initiative, enthusiasm and energy in developing the program and the plans for the carrying out of the congress, which bids fair to be an occasion of rare interest.

Correspondence

"COINCIDENCE OF LICHEN SCROFULOSORUM WITH LUPUS ERYTHEMATOSUS"

To the Editor:—In the March issue of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**31**:371, 1935), Montgomery recorded a case in which there occurred simultaneously lesions of lupus erythematosus and an eruption resembling lichen scrofulosorum; on the basis of this association, it was adduced that the former dermatosis is a tuberculid. Naturally, I am interested in such instances since they would tend to negate the conclusions which I drew from a study of the postmortem data in over 125 cases of the disease. Further necropsy studies (about 50 personally observed cases) have corroborated and strengthened my belief that there is no direct relationship between lupus erythematosus and tuberculosis.

In reviewing my paper for the 1934 "Year Book of Dermatology," Wise and Sulzberger, although not openly professing a belief in the relationship of the two conditions, did what all the adherents of this theory must now do to support the hypothesis; namely, they pointed to the coincidental occurrence of tuberculids with lupus erythematosus. In a later communication I shall discuss this topic in detail for the express purpose of showing the many difficulties encountered in the diagnosis of tuberculids, the many fallacies which have been overlooked or completely ignored and the numerous assumptions which have been taken for granted without an attempt at careful evaluation.

Lichen scrofulosorum is a cutaneous manifestation which in children is probably almost always tuberculous in etiology. It matters little whether the dermatosis arises from the effects of the bacillus itself or of its toxins; the fact remains incontrovertible that the eruption is found in patients manifesting undoubted evidence of the lymph node variety of the malady. Because it is practically restricted to this type of the disease, lichen scrofulosorum may be commonly seen in the various institutions devoted to the care of children with tuberculosis. So close is the association in my experience that if a carefully performed postmortem examination failed to disclose evidence of tuberculosis, I should be inclined to the view that an error in diagnosis had been made. In accordance with the evidence that the dermatosis is principally observed in the secondary period of generalization (Ranke), the eruption is uncommonly encountered in cases of pulmonary tuberculosis, a fact already known to Hebra, and consequently easily correlated with its relative rarity in adults in whom the lymph node variety of the disease is uncommon. Moreover, in adults there are greater opportunities for confusion with other dermatoses, such as "lichen syphiliticus" and especially the acute disseminated varieties of lupus erythematosus.

In 1914 Jadassohn, in a scholarly presentation of the subject of tuberculids, stated that the coincidence of lupus erythematosus with eruptions resembling those of folliclis (papulonecrotic tuberculids), erythema induratum and lichen scrofulosorum did not warrant the assumption of etiologic significance unless accompanied by *histologic* examination. Moreover, he cited an example of lupus erythematosus accompanied by lesions resembling those of lichen scrofulosorum in which the latter showed the typical microscopic picture of lupus erythematosus. The remarkable multiformity of appearance displayed by lupus erythematosus, especially by the acute disseminated varieties of the disease, has been known for many years

(Lewandowsky), and the possibility of confusion with tuberculids is readily recognized when one studies the minute anatomy in detail in terms of the gross attributes.

As there exists already so much confusion, it is imperative that all cases belonging in the category of associated eruptions be thoroughly studied before definite conclusions are reached.

H. KEIL, 509 Madison Avenue, New York.

DR. DOUGLASS MONTGOMERY'S REPLY

To the Editor:—The coincidence of tuberculids and lupus erythematosus is interesting and important principally as tending to show that lupus erythematosus is also a tuberculid. In the case reported in my paper both lesions were present at the same time and in juxtaposition, and both lesions were typical.

A considerable time has now elapsed since my article was submitted for publication, and the patient has greatly improved in general health with the administration of cod liver oil and iron and with attention to diet and to exercise. She could not tolerate gold preparations. Coincident with this constitutional improvement, the lesions of both types have improved, especially those of lichen scrofulosorum.

The coincidence of the lesions, their juxtaposition and their simultaneous involution are all strong, though not absolutely conclusive, arguments that they arose from a common cause.

Quite justly Dr. H. Keil requires that there should be no doubt regarding the diagnosis of lichen scrofulosorum and, particularly, that the lesions regarded as those of lichen scrofulosorum should not be really atypical lesions of lupus erythematosus. To my mind the eruption was typical. It consisted of papules with very little color, which were stationary and acuminate and were tipped with a corneous plug; they occurred in groups with no configuration and did not present any subjective symptoms. Each papule was separate from its neighbor, as can be seen in the photographs that appeared in the article, and this is an important point, as it might be inferred that the group over the ulna was really an atypical manifestation of lupus erythematosus and that if allowed to pursue its natural course the papules would coalesce and form a cushion-like lesion such as is shown near it. No such coalescence was noted, and in this respect the two eruptions differ widely. The lesions of lupus erythematosus tend to coalesce; those of lichen scrofulosorum tend to remain separate.

As for the lesions of the skin being syphilitic, there was nothing in their appearance or course or in the patient's history to support this theory. On the other hand, she had been exposed for years to tuberculosis in her husband.

In concluding, I fully appreciate the interest and the criticisms of Dr. Keil as those of a man conscientious in his craft and anxious to arrive at the truth.

D. W. MONTGOMERY, M. D., 450 Sutter Street, San Francisco.

Obituary

ROBERT HILL DAVIS, M.D.
1875—1934

Dr. Robert Hill Davis came of a distinguished Virginia family, and one whose history was linked, through its eminent members, with the University of Virginia. He was a great-great-grandnephew of Thomas Jefferson. He was the son of Dr. John Staige Davis Sr., who was professor of anatomy and materia medica at the University of Virginia and a brilliant lecturer. His mother was Caroline Hill. His brother, Dr. John Staige Davis Jr., who died in September 1933, was professor of pediatrics at the same university.

Dr. Robert Hill Davis was born on Sept. 14, 1875. He received his A.B. in 1898, his A.M. in 1899 and his M.D. in 1901, all from the University of Virginia. After pursuing his studies in Berlin and Vienna, he returned to this country and practiced at New Orleans for a year before coming to St. Louis in 1906. For some years he assisted the late Dr. William A. Hardaway at the dermatologic clinic of Washington University, St. Louis, and was assistant and instructor in dermatology from 1907 to 1912. He entered the department of dermatology of St. Louis University Medical School in 1913; he was appointed assistant professor of dermatology in 1922 and held the post of professor emeritus of dermatology at the time of his death. He was on the staffs of various hospitals, namely, the Bethesda General Hospital, the St. Louis Children's Hospital, the Barnard Free Skin and Cancer Hospital, the Jewish Hospital, the St. Louis City Hospital, St. Anthony's Hospital, St. Mary's Hospital and St. Mary's Infirmary.

He was a member of the St. Louis Medical Society, the Missouri State Medical Association, the American Medical Association, the St. Louis Dermatological Society, the Dermatological Conference of the Mississippi Valley and the American Dermatological Association.

Dr. Davis was married to Miss Ora May Lewis on Dec. 27, 1910. She died on April 24, 1931. A son and daughter survive them.

Dr. Davis retired from practice in September 1932 and in November of the same year returned to his old home at Charlottesville, Va., where he died on June 9, 1934.

He made several valuable contributions to dermatology, the best known being the Davis treatment of acute pemphigus, which was the first of any efficacy in this formerly hopeless disease.

Dr. Davis always conformed to the highest type of Christian gentleman. Ever deeply religious, modest and retiring, kind and benevolent, he preserved through life a serenity which could not fail to impress others. He was admired and beloved by all who knew him.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

JUVENILE PEMPHIGUS; TREATMENT WITH GERMANIN; REPORT OF A FATAL CASE. NORMAN TOBIAS, Am. J. Dis. Child. **48**:1084 (Nov.) 1934.

Tobias reports a fatal case of pemphigus in a white child aged 5 years. The patient lived for about one year after the onset of the disease. Various treatments were used, including a diet with a high vitamin content, the administration of viosterol, ultraviolet radiation, baths and acetarsone by mouth and two courses of injections of germanin. Remarkable clinical improvement followed the first course of four injections. The second course of four injections produced considerable improvement also.

Tobias gives a brief review of the literature on the therapeutic use of germanin.

ANDERSON, Los Angeles.

OUTBREAK OF ERYTHEMA INFECTIOSUM IN ELMSFORD, N. Y. PHYLLIS S. KERR and EDWARD H. MARSH, Am. J. Pub. Health. **23**:1281 (Dec.) 1933.

In the spring of 1933 an outbreak of twenty-five cases of erythema infectiosum was observed in Elmsford, N. Y. All the patients were between the ages of 3 and 13 years. Fever was seldom present, though there was occasional redness of the throat. The eruption consisted of a reticulated erythema which was usually found on the arms and legs but in a few instances was observed on the upper part of the trunk and on the neck. There was flushing of the cheeks in two cases, and one child had a distinct butterfly patch across the nose. There were four instances of multiple infection in one family. The period of incubation varied from four to fourteen days. No mode of transmission was determined.

McBRYDE, Durham, N. C. [AM. J. DIS. CHILD.]

EFFECT OF TRYPARSAMIDE ON THE EYE. N. K. LAZAR, Arch. Ophth. **11**:240 (Feb.) 1934.

There have been many reports concerning the effect of tryparsamide on the body since Jacobs and Heidelberger first produced the drug and since its use was introduced into the therapy of neurosyphilis. Few of these reports however, are based on experimental histopathologic study. Lazar made such a study and reported a case of blindness that was supposed to have been the result of treatment with tryparsamide. In addition, thirty-two cases of syphilis of the central nervous system in which this drug had been used were observed and are reported, with a review of the literature; opinions are presented which in some instances are contradictory.

Lazar draws the following conclusions relative to tryparsamide and its relationship to syphilis and the damage it may do in the eye: 1. Experimentally, one cannot demonstrate any histopathologic changes in the eyes, optic nerve, chiasm or brain of lower animals or of man which can with certainty be attributed to tryparsamide. 2. The definite loss of vision so soon after the injection of tryparsamide leaves no doubt of a definite toxic effect of the drug on the visual apparatus of certain patients. 3. Serious and even permanent damage may occur to a previously normal visual apparatus. 4. The tragic results which do occur from time to time illustrate the danger of giving the drug to persons showing evidence of atrophy of the optic nerve. 5. Persons to be treated with tryparsamide should be given a full ophthalmic examination, including examination of the visual fields, before treatment is instituted, and after the first three to six doses the fields should

be examined before another treatment is given. Atrophy of the optic nerve or evidence of constricted fields is a positive contraindication to the injection of the drug.

SPAETH, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

AN EOSIN-METHYLENE-BLUE TECHNIQUE FOR RAPID TISSUE DIAGNOSIS. EDWARD STEPHEN STAFFORD, Bull. Johns Hopkins Hosp. **55**:229 (Sept.) 1934.

A technic for rapid preparation of tissue is described. The time required for preparation of the complete section varies from five to seven minutes; the reagents used are relatively inexpensive, and the sections prepared by this method are permanent. The reagents employed and the method used were as follows:

(1) Fixing solution:
Dilute solution of formaldehyde, U. S. P. (15 per cent)... 75 cc.
Absolute alcohol ..... 25 cc.
(2) Eosin solution:
Eosin ..... 1 Gm.
Potassium bichromate..... 1 Gm.
Water ..... 100 cc.
(3) Methylene blue solution (Goodpasture):
Methylene blue..... 1 Gm.
Potassium carbonate..... 1 Gm.
Water ..... 400 cc.

Boil 30 minutes, add 3 cc. of glacial acetic acid, shake until the precipitate dissolves and concentrate to a volume of 200 cc.

(4) Dehydrating solution:
Absolute alcohol..... 1 part
Acetone ..... 5 parts
(5) Xylene
(6) Canada balsam

The sections were prepared as follows: Cut small thin blocks (not over 3 mm. thick) and heat to the boiling point in fixing solution in crucibles or test tubes. After washing freeze and cut into sections. Stain the sections for one second in eosin solution, wash in water, stain deeply in methylene blue solution for from ten to twenty seconds, again wash in water, then mount on slides. Blot the slides with blotting paper moistened with a drop of dehydrating fluid, dehydrate with dehydrating solution (from 15 to 20 drops), dip into xylene and mount in Canada balsam.

ANDERSON, Los Angeles.

AN INFECTIOUS DERMATITIS OF CERTAIN MARINE FISHES. CLAUDE E. ZOBELL and NELSON A. WELLS, J. Infect. Dis. **55**:299 (Nov.-Dec.) 1934.

ZoBell and Wells describe the pathologic changes of a highly fatal ulcerous dermatitis of Fundulus parvipinnis and other marine fishes. The disease is infectious, Achromobacter ichthyodermis being the etiologic agent. A study of the temperature requirements of the pathogen and its hosts has revealed that while the former can be acclimatized to multiply at temperatures as high as 38.5 C. (101.3 F.), when diseased fishes are transferred to an environment of 32 C. (89.6 F.) they rapidly recover from the infection. The hyperthermic treatment offers a satisfactory means of controlling the disease in aquariums.

SELECTIVE ACTION OF GENTIAN VIOLET ON ENZYMES. ALVIN Y. WELLS and NOBLE P. SHERWOOD, J. Infect. Dis. **55**:356 (Nov.-Dec.) 1934.

In previous publications Wells and Sherwood have shown the existence of a selective action of gentian violet and crystal violet on bacteriophages. The results obtained also present evidence that there is a correlation between the selective action of the dyes on bacteria and that on their respective phages.

Because several investigators have suggested the enzyme-like nature of the bacteriophage and because the two biologic substances present many similar properties, a study of the effect of dye on enzymes seemed to be a logical investigation to follow the aforementioned work on the action of dye on bacteriophages.

The chief objective in the experimental work reported in this study was to ascertain whether a similarity exists between the action of dye on bacterial enzymes and its action on the corresponding bacteria, as was found with the bacteriophages. The following observations were also noted: the effect of various reactions of mediums on enzyme activity and the quantity and speed of liquefaction of gelatin by the different enzymes.

The authors have demonstrated the existence of a selective action of gentian violet on bacterial gelatinase in a measure similar to that found for bacteriophages.

When a 1 : 400 dilution of gentian violet in acid medium was used, five of six gelatinases obtained from gram-positive bacteria were inhibited 100 per cent in from twenty-four to seventy-two hours, while the inhibition of the sixth varied from none at all to 25 per cent. On the other hand, of six gelatinases obtained from gram-negative bacteria, four showed inhibitions varying from none to 50 per cent, and two showed complete inhibition under similar conditions.

In this series trypsin was inhibited approximately 25 per cent.

The p_H range is rather wide for the bacterial gelatinases, including both acid and alkaline reactions. Gram-positive bacteria and their enzymes were inhibited to a greater degree in a low p_H than were the gram-negative group. The results obtained suggest a close relationship between the bacteria and their respective enzymes and bacteriophages. The enzymes from gram-negative bacteria were able to liquefy larger quantities of gelatin, and all the enzymes appeared to be more active in an alkaline medium.

BORDET-GENGOU AND LÖWENSTEIN MEDIUMS IN DETECTING TUBERCLE BACILLI IN SPUTUM: A SUBSTITUTE FOR GUINEA-PIG INOCULATION. LUCY MISHULOW, MARIO ROMANO, MILDRED MELMAN and CAMILLE KERESZTURI, J. Infect. Dis. **55**:402 (Nov.-Dec.) 1934.

Since guinea-pigs are susceptible to both human and bovine tubercle bacilli, inoculation of suspected material into these animals is one of the best methods of detecting the bacilli; but there are several difficulties connected with this method which make it impracticable for general use: 1. Guinea-pigs are susceptible to other infections and frequently die before tuberculous infection becomes manifest. 2. Other infections produce lesions which in some instances closely resemble tuberculous lesions, and, unless care is taken, a wrong diagnosis may easily be made. 3. Tuberculous infection in guinea-pigs will not take place unless there is a minimum number of virulent tubercle bacilli present; if there are fewer than the minimum number, infection may not take place and a negative result may be obtained. 4. Small laboratories, as a rule, have few or no facilities for keeping animals; also the expense of purchasing and maintaining them for from two to three months is an item that must be considered.

For these reasons diagnosis by means of inoculation of pathologic material into guinea-pigs is of necessity limited to specially equipped laboratories.

Diagnosis by means of culture instead of inoculation into guinea-pigs has recently been advocated by a number of workers. Two years ago Mishulow made a comparative study of the number of different mediums with the object of selecting one or more which could be easily prepared and could be stored for a long time and on which tubercle bacilli would grow rapidly and characteristically directly from pathologic material. It was found at that time that the Bordet-Gengou medium was well suited for this purpose. It was also found that the Löwenstein medium gives an excellent growth, especially of the human type of tubercle bacilli, and when used in conjunction with the Bordet-Gengou medium it is very helpful in determining the type of the tubercle bacilli.

The results were so encouraging that it seemed desirable to test the Bordet-Gengou and Löwenstein mediums further with a view of utilizing them in diag-

nosis, and, if the results warranted, to substitute culturing on these mediums for inoculation into guinea-pigs.

With this object in view, the authors carried out a group of investigations in which they found that the Corper-Uyei oxalic acid method of destroying non-spore-bearing contaminants in sputum gave better results than the sodium hydroxide method.

Culturing sputum on the Bordet-Gengou medium can be successfully substituted for inoculation of sputum into guinea-pigs in detecting small numbers of tubercle bacilli provided the specimens are not unduly contaminated with acid-resistant and alkali-resistant organisms. The Bordet-Gengou medium is especially advantageous in that it has simple ingredients, is easily prepared and can be stored for a long time. Tubercle bacilli of both human and bovine types grow freely and rapidly on this medium, and the growth of each type is very characteristic.

The Löwenstein medium when used in conjunction with the Bordet-Gengou medium is helpful in the further identification of cultures, as the human and bovine types of tubercle bacilli also give characteristic growth on this medium. The medium is helpful when available but is not necessary for isolation, as the Bordet-Gengou medium has given excellent results. The Löwenstein medium has the disadvantage of requiring special ingredients and a special method of preparation, and sometimes slowly growing contaminations, which may be due to the use of eggs in its preparation, crop up on this medium.

Culturing as a means of diagnosis has the special advantage of saving time and expense.

A Grouping of the Monilias by Fermentation and Precipitin Reactions. J. H. Lamb and M. L. Lamb, J. Infect. Dis. **56**:8 (Jan.-Feb.) 1935.

Tests for the fermentation of sugars were made by determining the presence or absence of the sugars after a period of incubation of four or five weeks with different strains of Monilia. By means of these fermentation tests and parallel precipitin tests of extracts of the organisms, the authors showed that there were three fairly definite groups of strains of Monilia: Group 1 comprises Monilia albicans, Monilia psilosis and Monilia candida. M. psilosis is included in this group because of its similarity in all reactions to M. albicans; M. candida, though not as closely related to M. albicans as M. psilosis, is closely related to this group according to the aforementioned tests and should be classified so as to show this close relationship. Group 2 comprises Monilia parapsilosis, which includes the fungus described by Stovall as Monilia type 1. Group 3 comprises Monilia Krusei, which is not closely related to any of the aforementioned species.

Tularemia in Wild Gray Foxes: Report of an Epizootic. Carl F. Schlotthauer, Luther Thompson and Carl Olson, J. Infect. Dis. **56**:28 (Jan.-Feb.) 1935.

Green and Francis have previously shown that foxes are not susceptible to tularemia. However, they experimented with red foxes. They definitely proved that this species is resistant to infection with Pasteurella tularensis. Schlotthauer, Thompson and Olson report a study on an epizootic of tularemia in wild gray foxes which occurred in southeastern Minnesota in 1933 and 1934. No sick or dead red foxes were observed.

Cornbleet, Chicago.

Hodgkin's Disease with Erythema Nodosum. C. J. Fuller, Brit. M. J. **2**:1172 (Dec. 22) 1934.

A man, aged 44, had an attack of erythema nodosum two months before the appearance of a glandular swelling in the neck. The swelling proved to be Hodgkin's disease. About a month later erythema multiforme appeared on the forearms.

TREATMENT OF BED-SORE WITH ELASTIC ADHESIVE PLASTER. THOMAS J. A. CARTY, Brit. M. J. **1**:105 (Jan. 19) 1935.

Two pieces of elastic adhesive plaster, one over the other, are applied so that the bed sore and an area of the skin surrounding it extending for 1 inch (2.5 cm.) are covered. The pieces are replaced when they no longer adhere—in the early stages of the treatment in from twelve to forty-eight hours—and on removal no attempt is made to clean the sore other than to wipe away the discharge. Carty states that in ten cases the results he obtained with this method were much better than those achieved with the usual methods of treatment. Fifteen days was the longest time that elapsed before healing, and in no case did the condition prove intractable. There was no systemic reaction from the retained discharge about the ulcer.

RATTNER, Chicago.

CUTANEOUS LESIONS OF LYMPHOGRANULOMATOSIS IN A WOMAN WITH A SYNDROME OF VULVO-ANORECTAL ELEPHANTIASIS. S. NICOLAU, Ann. de dermat. et syph. **5**:1 (Jan.) 1934.

A woman, aged 27, presented a syndrome of vulvo-anorectal elephantiasis of eight years' duration, with accompanying lesions on the buttocks and thighs but without involvement of the inguinal glands. Nicolau was able to prepare a vaccine from both the vulvar lesions and those on the buttocks which elicited a positive intradermal reaction in patients with lymphogranulomatosis inguinalis, in other words, a positive Frei reaction. Sections from the lesions showed a histologic structure compatible with a diagnosis of lymphogranulomatosis inguinalis. This case therefore conclusively demonstrates that the Nicolas-Favre disease may manifest itself in the form of cutaneous lesions alone, independently of inguinal suppuration.

ELECTIVE PRECOCITY OF THE KAHN REACTION AT THE BEGINNING OF SYPHILITIC INFECTION. ALICE ULLMO, Ann. de dermat. et syph. **5**:153 (Feb.) 1934.

From experiments with 8,000 serums, in which the Hecht-Bauer, the Bordet-Wassermann, the Vernes and the Kahn test were all made, Ullmo found the Kahn reaction to be the most sensitive of the four. She also observed that in twenty-four cases of chancre the Kahn reaction practically always became positive long before the others. From this Ullmo concluded that the preserologic period of syphilis, as determined by the Kahn test, is materially shortened.

GANDY, Houston, Texas.

EXPERIMENTAL TRANSMISSION OF SYPHILIS TO THE BOVINE SPECIES. ANTOINE BÉCLÈRE, Ann. Inst. Pasteur **53**:23, 1934.

Inoculation of the Truffi strain of spirochetes into the genital tracts of calves by various procedures was followed, in three or four weeks, by the appearance of small papules containing spirochetes. Transfers were made directly from human beings, although the adaptation was accomplished with greater difficulty.

MARSHALL, Kolhapur, India [ARCH. PATH.]

TWO INSTANCES OF FAMILIAL PSORIASIS. P. PHOTINOS, Bull. Soc. franç. de dermat. et syph. **40**:1437 (Nov.) 1933.

Two instances of familial psoriasis are reported. In one a young girl, her father and her grandfather were afflicted. In the other an old woman and her son suffered from the disease. Such instances again raise the question as to whether psoriasis is of external or of internal origin.

BROMODERMA IN A SUCKLING. SPILLMANN, WATRIN, WEIS and ROSENTAL, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Nancy) **41**:2 (Jan.) 1934.

A case of bromoderma in a nursling 7 months old is reported. The eruption was generalized but was most profuse on the face. The lesions were of the

vegetating, papulotuberculous type, some measuring 6 cm. in diameter. There were no subjective symptoms. The infant had been erroneously treated for syphilis for several weeks. The mother was taking bromides for epilepsy, and chemical analysis of her breast milk and urine disclosed bromide. Histologic study showed the usual picture of a vegetating bromoderma.

TREATMENT OF SCLERODERMA BY OVARIAN HEMOCRINOTHERAPY. A. SÉZARY and A. HOROWITZ, Bull. Soc. franç. de dermat. et syph. **41**:68 (Jan.) 1934.

A new method of treatment for scleroderma with which Sézary and Horowitz have had variable results is described. One case in which complete recovery took place is reported in detail, and a résumé of five other cases in which the results were good, bad and indifferent is given. Ovarian extract was added to 20 cc. of the patient's own blood and the mixture administered intramuscularly. The injections were given three times a week in courses of twelve. Sometimes improvement did not begin until the second or third course was given. The best results were obtained in patients approaching the menopause. In view of the scarcity of therapeutic resources against scleroderma the method is worthy of further trial.

COMPARATIVE TOXICITY OF SODIUM ACETARSONE AND ACETYLARSAN. A. SÉZARY and G. LÉVY, Bull Soc. franç. de dermat. et syph. **41**:78 (Jan.) 1934.

Sézary and Lévy found by experimentation that arsenic in the form of acetylarsan is three times as toxic to rabbits as arsenic in the form of sodium acetarsone.

SODIUM HYPOSULPHITE IN THE TREATMENT OF SCABIES AND VARIOUS CUTANEOUS CONDITIONS. RAVAUT and MAHIEU, Bull. Soc. franç. de dermat. et syph. **41**: 135 (Jan.) 1934.

Addition of an acid to a solution of sodium thiosulphate results in the precipitation of fine grains of colloidal sulphur. This fact is utilized by Ravaut and Mahieu in a new method of treatment for scabies. After a bath of soap and water the patient rubs on a 40 per cent solution of sodium thiosulphate and then applies a 4 per cent solution of hydrochloric acid. A deposit of sulphur forms on the skin. It is allowed to dry, and the procedure is repeated. The patient then dresses and goes about his occupation. The same operation is repeated the following day. Usually only two treatments are necessary, although the procedure may be repeated for several days in succession. It is a rapid, harmless, convenient and cheap method of treatment. Ravaut and Mahieu tested it on fifty-two patients with scabies (microscopically proved) which had been present from six days to six months; in fifteen of these patients other methods of treatment had failed, but perfect results followed the application of the new therapy. The authors found this procedure valuable also for other cutaneous conditions for which sulphur is indicated.

BILATERAL TUBERCULOUS INGUINAL ADENITIS CLINICALLY SIMULATING NICOLAS-FAVRE DISEASE. L. M. PAUTRIER and P. LANZENBERG, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **41**:218 (Feb.) 1934.

Pautrier and Lanzenberg report a case of inguinal adenitis in which lymphogranulomatosis inguinalis seemed the logical clinical diagnosis but the Frei test was negative and inoculation of a guinea-pig gave positive results for tuberculosis. This occurrence demonstrates the great value of the Frei test in revealing the presence or absence of Nicolas-Favre's disease.

A LITTLE SIGN OF MOLLUSCUM CONTAGIOSUM. A. TZANCK and PAUTRAT, Bull. Soc. franç. de dermat. et syph. **41**:237 (Feb.) 1934.

Molluscum contagiosum seldom offers any difficulties as to diagnosis, but a diagnostic sign claimed to be thoroughly reliable is offered by Tzanck and

Pautrat for the identification of doubtful cases. A fine jet of ethyl chloride is sprayed on the suspected lesion, and at the moment when whitening occurs a tiny crystalline circle, surrounding the lesion and sharply limited to it, stands out clearly. This phenomenon has been found to take place with remarkable constancy in cases of molluscum contagiosum and to be absent consistently in cases of other types of papules, such as warts and lesions of lichen planus, syphilis, etc.

TREATMENT OF PLANTAR WARTS. A. TZANCK and PAUTRAT, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **41**:238 (Feb.) 1934.

A method of treatment is proposed for plantar warts. The method is particularly adapted to the treatment of radioresistant and recurring types, and Tzanck and Pautrat claim to have obtained excellent results. Under local anesthesia the lesion is curetted, care being exercised to remove all the wart tissue without injuring the healthy tissue. One is able to differentiate between the two kinds of tissue by the "sensation of softness" imparted by the wart tissue and the resistance offered by the healthy tissue. Sometimes a deep cavity is produced. This cavity is filled with finely pulverized potassium permanganate. The hemostasis is instantaneous, and the pain which occurs after the disappearance of the anesthesia is of short duration. Recurrence of warts after this treatment is rare.

POSTTRAUMATIC NEVOCARCINOMA OF THE LEG. GOUGEROT and BURNIER, Bull. Soc. franç. de dermat. et syph. **41**:285 (Feb.) 1934.

Gougerot and Burnier report that malignant changes developed at the site of an injury eight months after the accident. In the discussion following the report Ravaut refers to the medicolegal aspects of such a case.

RETICULATED PEMPHIGUS. GOUGEROT and BLUM, Bull. Soc. franç. de dermat. et syph. **41**:287 (Feb.) 1934.

In a coppersmith, who was exposed to intense heat in his work and who had well marked pigmented livedo reticularis, pemphigus developed at the same sites, the sequence being: reticulated cyanosis (livedo), then pigmentation and finally pemphigus bullae. Gougerot and Blum regard this manifestation as another example of the "pemphigus reticules" described by Gougerot in 1919.

SWEAT GLAND EPITHELIOMA. H. GOUGEROT, ALBEAUX-FERNET and A. DREYFUS, Bull. Soc franç. de dermat. et syph. **41**:294 (Feb.) 1934.

A case of sweat gland epithelioma is reported because of the rare occurrence of the disease.

THE LEUKOCYTIC REACTION TO GOLD SALTS IN TUBERCULOSIS. THE CONDITION OF ACTIVITY OF GOLD PREPARATIONS IN CUTANEOUS TUBERCULOSIS. J. GOUIN, A. BIENVENUE, P. DESAUNAY and J. EZEL, Bull. Soc. franç. de dermat. et syph. **41**:310 (Feb.) 1934.

The leukocyte reaction to the injection of gold salts is specific, being positive in the presence of tuberculosis and negative in its absence. Of twenty-nine tests on nontuberculous patients not one was positive, twenty-seven being negative and two undetermined, and of seventy-two tests on tuberculous patients, seventy-one were positive. In cases of latent tuberculosis in which a clinical diagnosis cannot be made with certainty, a positive leukocyte reaction to gold salts can be accepted as establishing the presence of tuberculosis. The reaction is not interfered with by coexisting syphilis, but it is not constant in the presence of tuberculids; however, after the syphilis is removed by treatment the reaction may become positive. A positive reaction to gold salts is no guide as to success in treatment, as is true of the antisyphilitic remedies, and this is true particularly for cutaneous tuberculosis.

THE SECOND CONDITION FOR THE ACTIVITY OF GOLD PREPARATIONS IN CUTANEOUS TUBERCULOSIS. EXTERIORIZATION OF THE LESIONS. J. GOUIN and A. BIENVENUE, Bull. Soc. franç. de dermat. et syph. **41**:317 (Feb.) 1934.

The best results are obtained from the treatment of cutaneous tuberculous lesions with gold preparations when the lesions have been "exteriorized," i. e., subjected to the action of air and light. The method used by Gouin and Bienvenue was to scrape the lesions under anesthesia at the time of the initial injection and to leave them uncovered, scraping them again at succeeding injections when no cicatrization was seen. Gold sodium thiosulphate was used in doses of 0.15 Gm., and five or six injections usually sufficed for complete healing. There were no untoward reactions from this method, and cure was obtained in four of nine cases of disseminated tuberculous lupus, in two cases of lupus verrucosus, in five of six cases of tuberculous ulcer and gumma and in three cases of tuberculous adenitis.

TREATMENT OF HERPES ZOSTER BY INJECTIONS OF SULPHUR IN OIL. A. SÉZARY, A. MIGET and J. FACQUET, Bull. Soc. franç. de dermat. et syph. **41**:322 (Feb.) 1934.

Sézary, Miget and Facquet report a new treatment for the severe pain often associated with herpes zoster. The method consists of intramuscular injections of sulphur in oil, which produces a "shock effect." The authors used a special preparation of 1 per cent of sulphur in olive oil often employed in the treatment of dementia paralytica. The initial dose was 2 cc.; this was increased to from 6 to 10 cc. if necessary. The injections were given at two day intervals and were accompanied by the usual reactions of treatment by shock: fever, asthenia, general malaise, etc. Of six patients thus treated the results were excellent or very good in five. Because of the unpleasant reactions the method should be reserved for severe cases in which relief cannot be obtained by other means.

GANDY, Houston, Texas.

MILK DIET AND WATER METABOLISM IN CASES OF DIFFUSE CUTANEOUS DISEASES. G. F. CHIALE, Gior. ital. di dermat. e sif. **69**:1615 (Oct.) 1934.

A group of patients was placed on diet consisting exclusively of milk for seven days, the patients ingesting as much milk as they desired. At the end of the period a number of patients with pemphigus, Duhring's disease and lupus vulgaris showed no improvement, but a group suffering from generalized eczema, psoriasis and dermatitis arsenicalis showed marked improvement, the erythema, infiltration, exudation and edema being reduced to the point of a clinical cure. Experiments were carried out to estimate the metabolism of water when a diet consisting exclusively of liquids, such as that used in these cases, was given. Care was taken to include in the calculation the amount of water supplied by food, drink and the natural oxidation phenomena of the organism, as well as the amount of water excreted through the kidneys, intestines, lungs and skin. The individual volumetric characteristics and the protein content of the blood were also taken in consideration. These researches demonstrated that the water metabolism was highly disturbed in cases of diffuse dermatoses. The favorable effect of a diet of milk is explained by an increase in diuresis, with a corresponding diminution of hydremia and chloruremia, and by an increase in the osmotic pressure of the blood, draining of the tissues and elimination of liquids through the kidneys.

PSORIASIS AND URIC ACID. A SCARPA, Gior. ital. di dermat. e sif. **69**:1709 (Oct.) 1934.

Scarpa investigated the uric acid content of the blood, of the urine, of the normal and diseased portions of the skin and of the scales of ten patients suffering from psoriasis. Six patients with other cutaneous diseases were also subjected to the same investigation for purposes of comparison. Scarpa establishes the following points: 1. No alteration of the uric acid content of the blood and of the urine was

demonstrated in cases of psoriasis. 2. In some cases there is evidence of increased uric acid content of the skin in psoriasis compared with that in other dermatoses. 3. The uric acid content of the normal skin is greater than that of the skin affected with psoriasis, contrary to what is observed in other squamous dermatoses. 4. It seems that the difference in uric acid content between the portions of nonaffected skin and those of affected skin in cases of psoriasis is due to the greater amount of water in the latter, from which it is concluded that the difference is only apparent. 5. The uric acid content of the scales is high and is greater in psoriasis than in other dermatoses.

URIC ACID METABOLISM IN PATIENTS WITH PSORIASIS UNDER APURINIC AND HYPERPURINIC DIETS. J. LEVIN, Gior. ital. di dermat. e sif. **69**:1731 (Oct.) 1934.

Levin studied the uric acid content of the blood and of the urine of eight patients with psoriasis who followed an apurinic and a hyperpurinic diet alternately. The uric acid content of the blood was normal during the period in which no purin was ingested, and although it was increased during the period in which a diet rich in purin was followed, it was never above normal. During the time of both diets the uric acid content of the urine was within normal limits. Levin believes that patients with psoriasis suffer from abnormal retention of uric acid.

CUTANEOUS LESIONS OF LYMPHOGRANULOMATOSIS INGUINALIS. ALBERTO MIDANA, Gior. ital. di dermat. e sif. **69**:1743 (Oct.) 1934.

Midana reports a case of lymphogranulomatosis inguinalis associated with marked inguinal adenopathy and cutaneous lesions on the abdomen, the thighs and the gluteal regions, resembling ecthymatous pyoderma. An antigen made from the secretion from the cutaneous lesions gave strongly positive reactions in the same patient and in other patients with lymphogranulomatosis. Lesions were reproduced on the skin of the same patient by intradermal inoculation. Midana expresses the opinion that the virus of lymphogranulomatosis inguinalis may develop unusual dermotropic activity and may spread through the lymphatic system.

DYSTROPHIES AND MALFORMATIONS OF THE FINGERS IN HEREDITARY SYPHILIS. P. PINETTI, Gior. ital. di dermat. e sif. **69**:1755 (Oct.) 1934.

A woman, aged 42, presented numerous scars of gummas and sequelae of syphilitic arthritis of several joints. The most interesting finding was brachydactylia of both fourth fingers and shortening of the left fifth finger. Roentgen examination showed that the condition of the fingers was not a dystrophy but was caused by syphilitic disease of the bones dating from childhood.

EXTRAGENITAL CHANCROIDS. R. TEIXEIRA, Rev. méd. latino-am. **19**:1325 (Sept.) 1934.

Extragenital chancroids may arise from direct inoculation, or they may be secondary and result from auto-inoculation from genital chancroids. Chancroids of the latter type are by far the more common. Teixeira reports three cases of extragenital chancroids, located on the nose, the thumb and the internal surface of the thigh, respectively. He calls attention to the rarity of regional adenopathy in cases of extragenital chancroids. The treatment used by Teixeira consists of local therapy plus the intravenous administration of dmelcos vaccine.

PURPURA ANNULARIS TELANGIECTODES, MAJOCCHI. L. E. PIERINI and A. O. BONORINO, Rev. méd. latino-am. **19**:1331 (Sept.) 1934.

The authors report a case of purpura annularis telangiectodes, Majocchi, the second case of this rare dermatosis reported in Argentina in twenty years. The

patient, an Italian aged 33, had typical lesions on the legs and on the lower portion of the abdomen. Tuberculosis, cardiovascular disease and syphilis were ruled out. The cutaneous manifestations disappeared spontaneously in about six months. Histopathologic examination revealed lesions of endarteritis of the cutis. The only treatment used was a compression bandage on both legs.

PARDO-CASTELLO, Havana, Cuba.

THE MALARIAL TREATMENT OF TABETIC OPTIC ATROPHY. H. GASTEIGER, Arch. f. Augenh. **108**:471, 1934.

A series of patients with tabetic optic atrophy were treated by malarial therapy. In a few of the patients the ocular condition remained stationary for a time, or vision was lost rather slowly, but five of the patients suffered a rapid deterioration which seemed to be due to the treatment. In any event, there was no definite effect of the treatment in staying the tabetic process, and in view of the few cases in which the condition seemed to have been made worse Gasteiger believes that treatment with malaria cannot be recommended for tabetic patients whose optic nerves are damaged.

ADLER, Philadelphia. [ARCH. OPHTH.]

THE USE OF ACETARSONE IN CZECHOSLOVAKIA. KAREL HÜBSCHMANN, Česká dermat. **15**:1 (Jan.) 1934.

Acetarsone proved efficient in febrile and debilitated syphilitic subjects and in those for whom intravenous therapy was inadvisable. The indications for the use of acetarsone were enlarged to include the prophylaxis of syphilis, other chronic dermatoses in which a solution of potassium arsenite ceased to be efficacious, especially psoriatic arthropathies, certain anemias and states of debilitation, fusospirillar infections, pyorrhea, frambesia, bronchial spirochetosis, etc.

SPINKA, Texarkana, Texas.

INVESTIGATION OF RATIONAL METHODS OF EXTERNAL TREATMENT OF CUTANEOUS DISEASES. M. A. AGRONIK, Sovet. klin. **20**:68, 1934.

Agronik considers the enormous use of ointments and pastes unjustified, for as vehicles of drugs they do not penetrate into the intact epidermis, and even when the epidermis is damaged the resorption of the effective drug is small and this necessitates the use of drugs in high concentration. In consequence of physicochemical properties ointments and pastes may make the cutaneous condition worse or retard healing, for they disturb the p_H of the skin necessary to protect it against saprophytic organisms. Their use is inconvenient and is frequently more bothersome than the illness itself. Solutions and lotions are more economical and convenient and, when not contraindicated, are preferable to ointments and pastes. Sulphur, which is being used extensively in dermatologic practice but which is not soluble in water or alcohol, may be used in the form of sodium hyposulphite in combination with a 5 per cent solution of hydrochloric acid, the one solution being used in the morning, the other in the evening. Through this combination free sulphur or sulphur gas is produced which acts favorably, according to Agronik, on many conditions for which sulphur is indicated, such as erythrasma, pediculosis capitis and pediculosis corporis.

THE CLINICAL PICTURE OF PELLAGRA. L. I. VILENSKIY and V. A. POSPELOV, Sovet. klin. **20**:105, 1934.

Vilenskiy and Pospelov express the belief that undernourishment does not play a rôle in the etiology of pellagra, for among one hundred and eight patients studied only twenty-four had had insufficient nourishment, and they saw no cases of pellagra during the famine of 1921 in Povoloje. The appearance of pellagra in spring and summer and its disappearance in winter indicate a sensitization to sunlight. Avitaminosis apparently plays a great rôle because of wrong methods

of preparation of food during the winter, which destroy thermolabile vitamins. The etiologic rôle of alcohol could not be confirmed by the authors except in a few cases.

The authors divide their cases into two groups: one in which cutaneous and general somatic symptoms and one in which mental and nervous symptoms predominated. Of one hundred and eight patients with pellagra, eight died; three of these had the typhoid form of pellagra, and five had intercurrent pneumonia.

In the first group there was marked involvement of the gastro-intestinal tract with changes in the mucous membrane of the tongue producing a so-called "bald tongue" and "chess-board" tongue. In 20 per cent of the cases there were excoriations of the mucous membranes of the cheeks. In all the cases there was complete absence of free hydrochloric acid and combined acidity. The patients showed marked salivation.

The covered parts of the skin were affected. There was frequently an erythematous triangle the base of which was formed by the manubrium sterni and the apex by the middle of the chest. In some cases the erythema of the hands and feet extended to the elbows and knees. The authors also observed several cases of involvement of the neck and chest in the form of Casal's collar. In some cases the erythema lasted three days and was followed by pigmentation; in others the erythema persisted until the end of the illness and was associated with hyperkeratosis and other cutaneous changes.

The histologic examination in two cases revealed no increase of pigment in the basal layer of the epidermis. Pigmentation is due, according to Vilenskiy and Pospelov, to discoloration of the corneous layer and the hyperkeratotic tissue. This theory was confirmed clinically, for the skin underlying the scales and the hyperkeratotic layer showed normal color.

The treatment administered by the authors consisted of a diet rich in vitamin B_2, which is contained in great amounts in liver, kidneys, milk, eggs, butter and fish fat. Some of the patients received from 15 to 30 Gm. of dry yeast per day.

CLINICAL OBSERVATIONS IN PELLAGRA. I. I. SNISARENKO, Sovet. klin. **20**:113, 1934.

Of 387 cases of pellagra recorded in the city of Piatigorsk 75 occurred in children. One hundred and thirty cases were observed by Snisarenko at the dispensary for diseases of the skin.

The majority of patients had diarrhea for from one to two weeks before the appearance of cutaneous symptoms; a few had diarrhea for from one to six months before. Fifty-seven patients had involvement of the lips; 70, of the tongue, and 30, of the mucous membranes of the mouth. A few patients had no cutaneous eruption at all (pellagra sine pellagra). The erythema on the dorsa of the hands reached as far as the end of the first phalanx of each finger; in 12 there was involvement of the second and third phalanges. In a few there was extension of the erythema from the dorsal aspects of the wrists and from the dorsa of the feet and legs to the flexor surfaces. Casal's collar was noted in 2 cases. Although the large majority of patients wore shoes, the skin of the extensor surfaces of the feet and legs was affected. Of 9 patients with vulvitis 7 were children. Few showed involvement of the nerves.

Of the 130 cases observed by Snisarenko 39 were mild, 51 severe and 40 very severe. Forty-one patients died.

BLOOM, New York.

STUDIES ON THE PROVOCATION REACTION IN SYPHILIS: I. CLINICAL OBSERVATIONS. KATSUJI OHASHI, Jap. J. Dermat. & Urol. **36**:27 (July) 1934.

The provocative agents injected consisted of arsenicals, bismuth preparations, gold preparations and therapeutic malaria vaccine. The clinical material consisted of sixty patients with syphilis of various types and in various stages and a few nonsyphilitic patients as controls. The response to provocation was most marked

in the primary and secondary stages (namely, in the early stages) and in cases in which the serum reaction was already positive. The most effective preparations in this regard were the arsenicals and bismuth. In the more markedly positive cases the response tended to set in within the first week, and the more intense response was frequently of long duration.

A previous cure exerted an interesting influence on the response: The more inadequate the treatment the more frequent was the response, although untreated patients did not exhibit a high percentage of responses. The tendency to respond was more pronounced in cases in which the last antisyphilitic medication had been of recent date (within one year), the tendency slowly diminishing, to finally rise again after a long period.

BRENNAN, Chicago.

EXPERIMENTAL YAWS IN MICE: III. REINFECTION EXPERIMENT. H. MISAIZU, Lues: Bull. Soc. japon. de syph. **11**:1 (June) 1934.

Mice which had been infected with yaws thirty, two hundred and forty-five and three hundred and twenty-eight days previously were treated with sodium arsphenamine, receiving three doses (0.001 Gm. per ten grams of body weight) every day for 3 days. Twenty days after the last injection they were reinoculated with yaws. Reinfection took place in most of the mice. This experiment proves that immunity against reinfection in yaws is almost nil.

DISPOSITION AND CURABILITY OF SYPHILIS IN RELATION TO BLOOD GROUPS. M. NISHIMURA, Lues: Bull. Soc. japon. de syph. **11**:15 (June) 1934.

Nishimura has investigated the blood grouping in 7,293 syphilitic Japanese men and women, 562 of whom he examined himself. The data for the others were taken from the Japanese literature. No relation between blood grouping and a disposition to syphilis was noted.

In 75 recognized cases of primary syphilis in which a Wassermann test was made four weeks after the first course of treatment, it was found that patients whose blood belonged to the groups O and A showed a higher percentage of negative reactions than those with blood of groups B and A B.

CHANGES IN THE CONJUNCTIVA IN EARLY STAGES OF SYPHILIS. K. HOSHINA, Lues: Bull. Soc. japon. de syph. **11**:31 (June) 1934.

Hoshina has found in the literature reports of 137 cases of early syphilis associated with changes in the conjunctiva. The changes consisted in diffuse congestion, inflammation and edema, nodular eruption, diffuse infiltration and conjunctivitis granulosa syphilitica.

He has observed fourteen patients with early syphilis who showed such changes in the conjunctivae.

BLOOM, New York.

DIPHTHERIA OF THE SKIN. AAGE KRISTJANSEN, Hospitalstid. (supp.) **76**:17 (Dec. 21) 1933.

A 5 year old boy had a severe form of prurigo of the Besnier type, with pronounced eczema of the face and scalp, which had proved resistant to all ordinary treatment. In the third and fourth years of his life he had made frequent transfers between the hospital for diseases of the skin and the hospital for contagious diseases. Invariably examination at the former revealed the presence of diphtheria bacilli in the discharge from the nose and throat and at the roots of the hairs, and he was transferred to the latter. When examination at the hospital for contagious diseases no longer showed diphtheria bacilli he was sent back to the hospital for diseases of the skin, whence after a few weeks or months he was returned to the hospital for contagious diseases. When he was seen by Kristjansen diphtheria bacilli were found at the roots of the hair. There could be seen and

felt numerous nodular infiltrations, groups of follicular pustules and tiny abscesses; on puncture the abscesses proved to be filled with pus containing diphtheria bacilli. The bacillary infection was refractory to treatment with poultices, salves, sulphonated bitumen, serum and other remedies. An epilation dose of roentgen rays was applied, and afterward the scalp was painted with a 1 per cent solution of acriflavine hydrochloride, which caused the pustules to dry up completely. At the Municipal Serum Institute three months later the skin yielded rolls of diphtheria bacilli, cultivation of which produced a very toxic virus.

VINTON, Brooklyn. [AM. J. DIS. CHILD.]

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

E. William Abramowitz, M.D., *Secretary*

Nov. 7, 1934

R. H. Rulison, M.D., *Chairman*

Dermatitis Medicamentosa (Chloral). Presented by Dr. Louis Tulipan.

E. B., a woman aged 65, has a rash which appeared a few days after she had taken a mixture of bromides and chloral hydrate for insomnia. This occurred ten days ago. On the back and chest were confluent patches of bluish, erythematous macules. Around the periphery were discrete macules. The face, especially the part around the eyes, showed erythema and edema. The macules were somewhat edematous. With the exception of desquamation, the rash had practically disappeared by yesterday, when the patient took another teaspoonful of the mixture of bromides and chloral hydrate containing 5 grains (0.32 Gm.) of chloral hydrate. One hour later there developed severe itching, and shortly afterward an exacerbation of the rash appeared. The patient now presents a closely aggregated erythematous, macular eruption of scarlatiniform pinpoint lesions on the trunk and arms. There is edema of the face, particularly of the region around the eyes, as in the original eruption. Desquamation from the first attack is still present.

DISCUSSION

Dr. Herman Sharlit: Is Dr. Tulipan certain that no other chemicals than bromides and chloral hydrate are contained in the mixture? This history is suggestive of ingestion of quinine, and quinine causes scarlatiniform eruptions.

Dr. Louis Tulipan: The mixture was given to the patient at the hospital. It is a regular formula containing chloral hydrate and bromides.

Dr. Edward R. Maloney: Dr. Tulipan is somewhat mistaken as to the history. The patient has been taking the mixture of chloral hydrate and bromides for some time for hypertension. She had taken it probably for a couple of weeks before the original eruption broke out; the rash was not caused by just one dose, as was stated in the history. However, the second eruption developed after one dose only.

Dr. E. William Abramowitz: Dr. Noun and I reported (*J. Allergy* **4**:338 [May] 1933) an interesting case of an eruption resulting from exposure to chloral. The patient was a druggist. He presented at first an eczematous eruption on the hands; later swelling of the face and extension of the eruption on to the body developed. We suspected that the eruption was caused by an external agent, and patch tests demonstrated that the patient was sensitive to chloral hydrate. A test with 1 per cent chloral hydrate caused a cutaneous reaction of 4 plus grade. After we obtained that reaction, the patient told us the following story: A physician in his neighborhood prescribed chloral hydrate for nearly every patient whom he visited. This druggist filled about fifteen of these prescriptions daily, and evidently he became sensitized in handling the drug. We proved this on several occasions, as he was inclined to doubt the cause of his cutaneous eruption. He had no further recurrence after he avoided handling chloral.

In looking up the literature we found that there are few reports of cases of cutaneous disturbances following the internal use of chloral hydrate and even fewer cases of reactions from external use of the drug. This, of course, does not include

direct irritation from strong ointments containing chloral. It is interesting to note that Dr. Tulipan's patient stated that she had hay fever twenty years ago.

DR. MARION B. SULZBERGER: This patient has had hay fever, but I do not believe that this is necessarily connected with the type of eczematous eruption due to a drug which she exhibits. In general, there seems to be no connection between sensitivity to drug and hay fever. I have not found the two conditions to be more frequently associated than one would expect by the laws of chance. Most students of allergy share that opinion. In their practice with atopic patients they do not find an association between atopy and sensitivity to drugs any oftener than we do.

PUSTULAR PSORIASIS. Presented by DR. DAVID BLOOM.

CASE 1.—Mrs. R. H., aged 70, was previously presented at a meeting of the New York Academy of Medicine, Section of Dermatology and Syphilis, in November 1933 (ARCH. DERMAT. & SYPH. **29**:757 [May] 1934). She had been suffering from an eruption on the palms and on the plantar surface of the heels and toes for thirteen years. The lesions never disappeared entirely.

CASE 2.—R. B., a woman aged 27, of Polish Jewish parentage, was first seen in the clinic for cutaneous diseases of the Bellevue Hospital on Jan. 7, 1931, with an eruption on the palms and soles which had appeared six months previously. It started on the proximal part of the thenar eminence of the left hand. Later it appeared on the right hand and then on the soles. The eruption consists of flat pustules from the size of a pinpoint to that of a pinhead on an erythematous, somewhat scaly skin. The patches are well defined; at present they are situated in the middle of the sole and also involve the instep and the lateral part of the feet. One quarter-sized patch is located on the medial side of the right ankle. The nails of both large toes show yellow discoloration at the sides and at the center. The nails of the fingers show pitting and longitudinal ridging.

The feet were examined for fungi on two occasions, but none were found. Microscopic examination of the skin of the foot was reported as follows: "There is slight acanthosis with formation of a hyperkeratotic scale, diminution of the granular layer, intercellular edema, some spongiosis and slight inflammatory round cell reaction. These findings are consistent with the picture of psoriasis. However, the absence of parakeratosis and of Munro abscesses and the lack of clubbing and fusion of the pegs and high rising papillae force the conclusion that the final diagnosis rests with the clinician."

Treatment with ointments or roentgen radiation has been of no avail. Spontaneous disappearance or improvement of the lesions is soon followed by a recurrence or exacerbation.

Roentgen examination of the teeth showed them to be in perfect condition. The tonsils are somewhat enlarged but do not seem to be infected.

DISCUSSION

DR. ISADORE ROSEN: This condition has been discussed often at meetings of dermatologic societies, and there seems to be a great deal of doubt regarding the existence of pustular psoriasis. Some dermatologists prefer the designation psoriasis with pustules to that of pustular psoriasis. There is one point I should like to emphasize; namely, that occasionally vesicles are present in the early stages of the malady and therefore a clinical diagnosis of dermatomycosis is made. However, when the lesions are examined microscopically and when cultures are made the results are always negative. If the patients are kept under observation for some time it is seen that ultimately pustules develop. The presence of vesicles in psoriasis is denied by some dermatologists, but there is no question about it in my mind. Dr. Bloom states that there were vesicles in his cases, and the members have noted several cases of such eruptions that undoubtedly began with vesicles. The pustules are not superficial but deep-seated. I have a patient whose condition I diagnosed as dermatomycosis; after two visits he stayed away for six months.

When I saw him again he presented a typical example of psoriasis with pustules. He also had psoriatic lesions on the trunk and scalp. To my mind it is immaterial whether the disease is named pustular psoriasis or psoriasis with pustules; perhaps the latter designation will satisfy all the dermatologists.

DR. EUGENE F. TRAUB: All the members have seen quite a number of such cases in the past, and Dr. Andrews and Dr. Kelly perhaps have the correct idea in not attempting to make a specific diagnosis in these cases until more certainty of their relationship to psoriasis exists. The two patients presented tonight show no evidence of ordinary psoriasis on any part of the body. I recall no case of ordinary psoriasis in which this type of lesion was present on the hands and feet. Microscopic examinations cannot be relied on either for making a diagnosis of psoriasis or for excluding it in these cases. I do not deny that these may be cases of pustular psoriasis, but I should like to see a little more proof before accepting this diagnosis. Some years ago I had a patient who handled cattle who had similar lesions. Dr. Williams found tinea of a type peculiar to cattle. In another similar case that my co-workers and I observed for a number of years the condition in some of that patient's lesions was rebellious to treatment but cleared up entirely after a thyroidectomy. Of course, the fact that the lesions are often associated with focal infection does not help in making a diagnosis. It seems that further study as to the etiology should be undertaken before a final opinion is reached.

DR. ANTHONY CIPOLLARO: I agree with the diagnoses that were presented. Both patients have pustular psoriasis as described by Barber. In describing such cases, Barber differentiated the condition from acrodermatitis continué of Hallopeau and from dermatitis repens of Crocker, which usually begins with trauma or a slight infection and gradually spreads peripherally. The primary lesion of pustular psoriasis is a pustule and not a vesicle. The pustule is deep-seated and has a flat top; it is not dome-shaped like ordinary pustules. When the material from the pustule is cultured it is always sterile. Fungi are not found in any of the scrapings from such lesions. The pustules are symmetrically placed on the palms and soles and are extremely recalcitrant to treatment. Some may respond temporarily to treatment with chrysarobin, mercury, salicylic acid and tar, to roentgen irradiation, to removal of tonsils and to other procedures. They run a chronic course. In the past three years I have had an opportunity to observe nine cases, which have been followed continuously ever since. The histologic pictures in all the cases my co-workers and I studied did not show typical psoriasis. In some the picture was that of eczema; in others it was suggestive of psoriasis. In some of the cases psoriatic lesions of the nails, scalp or body developed later. Whether these lesions can be classified as pustular bacterids, the name Andrews suggested, needs further consideration.

DR. T. J. RIORDAN: The criteria for a histologic diagnosis of psoriasis are well known. Unfortunately they are not found in all specimens. I notice that in most of the cases in which the condition is diagnosed as psoriasis with pustules or pustular psoriasis the tissue presented for examination is from the palms or soles. I also note that the so-called Munro abscess is found more often in tissues from the palms and soles. In one or two cases of pustular psoriasis, in which the condition was regarded as pustular, I found an agglomeration of a Munro abscess in the corneous layer or at the junction of the granular layer and the corneous layer, which is the usual site of a Munro abscess.

DR. GEORGE M. LEWIS: It seems that the two patients show different types of eruptions. The lesions to be seen in the first are typical of a frank pustular psoriasis. In the second, the primary lesions appear to be vesicular pustules arising from normal skin. There is an associated interdigital dermatomycosis, which is a positive clinical finding that speaks against any evidence of psoriasis elsewhere. I advise that this case be studied again and that the possibility of a fungous infection be kept in mind. The absence of mycologic findings means little unless the examination is repeated several times. The fact that the disease is recalcitrant

to treatment does not necessarily mean that it is pustular psoriasis. In many cases dermatomycosis has lasted for many months and even years without being cured.

DR. DAVID BLOOM: My co-workers and I have observed seven cases of pustular psoriasis of the palms and soles. In several cases there were lesions between the toes which looked exactly like those seen in dermatomycosis, but we never found fungi in the scrapings. I do not know of any other lesions which respond so little to roentgen therapy as those of pustular psoriasis. This trait agrees with the characteristics enumerated before as arguments that this type of eruption is a separate entity. On looking over a number of reports of cases in the literature one finds that the eruption was associated with typical psoriasis of other portions of the skin. The effect of removal of focal infections on the eruption does not argue against pustular psoriasis. In two of our cases there was a typical histologic picture of psoriasis. The pustules were seen as a conglomeration of Munro abscesses.

LATE STAGE OF SECONDARY SYPHILIS SIMULATING LUPUS VULGARIS. Presented by DR. H. C. SAUNDERS.

H. S., a man, aged 31, is presented from the clinic for cutaneous diseases of the New York University and Bellevue Hospital Medical College because of an eruption on the back, right arm, left shoulder, left breast, right index finger and right hip. He had tuberculosis of the right ankle joint at the age of 2 years. In December 1933, there developed a cervical adenitis, followed by a maculopapular eruption; both conditions responded to treatment. The Wassermann reaction of the blood was 4 plus. He received sixteen injections of neoarsphenamine, thirty of a bismuth preparation and four of mercury. He also had fourteen inunctions with mercury. The injections of neoarsphenamine were discontinued because of severe nitritoid reactions. The Wassermann reaction of the blood has been persistently positive.

After the sixth injection of neoarsphenamine the lesions which are now present appeared. They were not influenced by subsequent treatment. On the back, there is an irregularly oval area, 10 by 14 inches (25.4 by 35.5 cm.), composed of numerous hard lentil-sized papules of the color of raw ham; some of the papules are capped by a small scale. There are a few soft papules which on pressure seem to be invaginated and to have a central depression. All are flat and for the most part discrete. There is some clearing of the center of the patch. The other involved areas resemble the one described but are smaller. The border of the eruptive area on the hip is formed by segments of circles. The center is clear and brown. The lesions on the forefinger show no distinct papules and are covered by a thick scale.

Roentgen examination of the right ankle showed ankylosis of the joint, with no active lesions. Roentgen examination of the lungs gave negative results. A test with old tuberculin (1:100,000) elicited a strongly positive reaction. The biopsy report was "syphilis."

DISCUSSION

DR. LOUIS CHARGIN: I hesitate to offer a positive diagnosis in this case, principally because this patient fails to respond to antisyphilitic treatment. I should say that the condition resembles syphilis more than lupus vulgaris. Lupus vulgaris would take much longer than a few weeks or months to develop. Moreover, on analyzing the configuration of the eruption one would be inclined to regard the disease as syphilis rather than as lupus vulgaris. On the other hand, if the history as stated by Dr. Saunders is correct, one would hardly expect an eruption of this type at this stage of syphilis, that is, after the disease has been present for six or seven months. It is really difficult to offer a positive diagnosis in this case.

DR. ISADORE ROSEN: I do not think that I can add much to the suggestions made by Dr. Chargin. Clinically the condition shown by this patient suggests to me lupus vulgaris rather than syphilis. I thought that the man had had some

external applications which produced a secondary dermatitis which altered the clinical features. I cannot conceive of the development of this type of syphilis while the patient is under systematic treatment. It is possible, however, that as a result of the syphilitic infection the old tuberculous process has been activated and that the lesions therefore are some form of tuberculosis or tuberculid.

Histologically it is difficult at times to differentiate between tuberculosis and syphilis. I remember that ten or twelve years ago at the Vanderbilt Clinic I saw with the late Dr. Fordyce a patient who had a large raised, soft, tumid patch on the posterior portion of the chest which clinically and histologically resembled lupus tumidus. On further investigation we found that the man had a strongly positive Wassermann reaction, and after antisyphilitic therapy had been administered for six or seven weeks the condition cleared up entirely. At that time, Dr. Fordyce, who had had an unusually large experience in studying tuberculous and syphilitic tissue, emphasized that in certain instances it is impossible to distinguish between these two diseases unless either the tubercle bacillus or the spirochete is found.

Dr. A. Benson Cannon: I am inclined to accept the diagnosis of syphilis for the reasons given by Dr. Chargin. On the other hand, I believe that, as Dr. Rosen has pointed out, it is not possible to distinguish between tuberculosis and syphilis of the skin when lesions such as those of this patient are present. The members may recall that a few months ago at a meeting of this section I presented a patient with a lesion on the nose and lesions on the scapulae and the buttocks. Most of the members diagnosed the condition as syphilis. The Wassermann reaction was persistently negative, and the lesions failed to respond to antisyphilitic treatment. A guinea-pig inoculated with tissue removed from one of the lesions died of tuberculosis, and tubercle bacilli were isolated from the organs of the guinea-pig. The patient was finally cured after the tuberculous areas had been removed by cautery. The members probably remember the patient who has been at the New York City Hospital for more than twenty years with an extensive tuberculous involvement of the skin extending over the buttocks and lower extremities. That eruption was at first diagnosed and treated as syphilis, later it was treated as tuberculosis for many years. Often it is equally difficult to distinguish histologically between a serpiginous ulcerating tuberculous lesion and a similar lesion caused by syphilis. As it is known that this patient has had tuberculosis, that there is a history of syphilis and that the Wassermann reaction is strongly positive, I do not think it is important to determine at present whether the ulcerations are caused by tuberculosis or by syphilis. It seems to me that the thing to do is to give the patient active antisyphilitic treatment and to inoculate a guinea-pig with a portion of the tissue removed from one of the lesions. I remember well the patient that Dr. Rosen mentions having seen at the Vanderbilt Clinic with Dr. Fordyce a number of years ago. His lesions never entirely disappeared, and he still comes to the Vanderbilt Clinic to be treated for lupus tumidus. The diagnosis of tuberculosis was finally established by inoculating a guinea-pig. The patient still has a negative Wassermann reaction of the blood.

Dr. Charles Wolf: The discussion has brought out evidence that the lesions are not due to syphilis. I should like to make a tentative diagnosis of tuberculid of the lichen scrofulosus type. There are lesions at the outskirts of the main portion of the eruption which are lichenoid papules. The fact that the patient had tuberculosis of the ankle joint indicates that this eruption is more likely a tuberculid than a manifestation of primary tuberculosis such as lupus vulgaris.

Dr. Sigmund Pollitzer: It is sometimes difficult to make a differential diagnosis between tuberculid and syphilid, both clinically and histologically. My own impression of this case, regardless of the history but purely from clinical examination, is that the eruption is a late nodular or large papular syphilid. I cannot conceive of a tuberculous reaction as extensive or widespread and as obviously acute as these lesions seem to be occurring in so short a time without producing more profound systemic changes. That fact alone leads me to doubt the correctness of the diagnosis of tuberculosis. Why this man has not responded better to antisyphilitic treatment, I do not know. Perhaps if the treatment is continued it will produce an adequate response. How much treatment has the patient had?

DR. H. C. SAUNDERS: He had sixteen injections of neoarsphenamine, thirty of a bismuth preparation and four of mercury.

DR. SIGMUND POLLITZER: I am much surprised that he has shown no response. I can conceive of such a thing happening for some reason or other, but I cannot conceive of tuberculosis developing to this extent in such a short time without evidence of stormy systemic disturbances. On clinical grounds alone I believe that the eruption is a syphilid.

DR. LOUIS TULIPAN: Stokes mentioned that in cases of this type eruptions consisting of nodular lesions and even resembling lesions of tertiary syphilis develop during a course of treatment. I have seen such cases myself. There is no reason to rule out syphilis just because the eruption occurs at this stage. I believe that the patient has a syphilitic eruption.

DR. PAUL GROSS: The two arguments pointing against the diagnosis of syphilis cannot stand up under close scrutiny. As far as the stage is concerned, I have, for instance, seen a typical gumma appear about three months after the patient had been insufficiently treated for an eruption of early secondary syphilis with iritis. The lack of response to antisyphilitic treatment has been repeatedly demonstrated, and I again had occasion to convince myself last year that such lack of response occurs. I saw a patient with palmar and plantar syphiloderm and mucous patches which appeared shortly after three and a half courses of combined antisyphilitic treatment given in a good institution. The most important point against tuberculosis was brought out by Dr. Pollitzer. Such an extensive eruption of such short duration—and, of course, the clinical picture could be compatible only with the diagnosis of lupus vulgaris—would be associated with some systemic disturbances.

DR. T. J. RIORDAN: The histologic report is helpful although it may confuse the issue somewhat. I approached the study of this tissue with bias because from the clinical picture I thought that the disease was lupus vulgaris. Lupus vulgaris is one type of tuberculosis that histologically is not confused with syphilis. The picture found was not that of lupus vulgaris. The infiltration consisted mainly of lymphocytes. There was a proliferation of fibrous tissue, the blood vessels were closed and most of them showed a dense collar of lymphocytes. The only conclusion one could draw was that the material gave definitely more evidence of syphilis than of tuberculosis. The only changes suggestive of tuberculoid structure were the presence of a few epithelioid cells and, in places of denser infiltration, a paucity of blood vessels. These changes may help to explain the process as a latent tuberculid activated by syphilis. There is no doubt about the syphilitic condition of the blood vessels and the changes in the fibrous tissue.

DR. EUGENE F. TRAUB: A point that may be of some importance in this case has not been mentioned, namely, the fact that the patient was suspected of having had an extragenital chancre. It has been mentioned a number of times in the literature that often these patients with extragenital infection do not respond as well to the usual amount of antisyphilitic therapy. I treated a patient with this kind of infection, and lesions and bony changes of late secondary syphilis developed during several courses of treatment. The extragenital chancre, therefore, may be one of the factors that accounts for this patient's responding so poorly to treatment. The polymorphous character of the eruption and its comparatively short duration make syphilis the more likely diagnosis.

DR. MARION B. SULZBERGER: Enough has been said to show that this patient has an atypical eruption of some kind. When I first saw him, I made a diagnosis of some type of granuloma. That is not an exact dermatologic diagnosis, but I think that it is as far as one can go with any degree of certainty, clinically or histologically. The rest depends on further studies, immunologic and so on, and especially on inoculations of animals. I do not think that the fact that the condition has not responded to antisyphilitic treatment has great weight in ruling out syphilis. Atypical syphilitic eruptions are likely to be atypical in other things than their appearance; that is, they may be also atypical in their response to therapy.

Stokes brought out that point. Most of his cases in which there was no response to treatment were morphologically atypical (psoriasiform, etc.).

I think the question of tuberculid should be carefully considered because a tuberculid can appear suddenly, can be widespread and still not affect the general health of the patient and can be activated by some other disease. However, I do not agree with Dr. Wolf that this may be lichen scrofulosus. It has none of the clinical characteristics of lichen scrofulosus. It must be some other unusual form of tuberculid if any. However, as I said before, I do not believe that more definite conclusions can be reached without laboratory studies.

Dr. Hermann Goldenberg: I cannot make a diagnosis. I do not know what type of granuloma it is, but I agree with Dr. Sulzberger that it is probably a tuberculid.

Dr. David Bloom: A few years ago I presented here a woman in whom there developed, while she was receiving antisyphilitic treatment, a generalized eruption which was found to be a tuberculid. I now have a patient under observation, a Negress who while receiving antisyphilitic treatment exhibited an extensive eruption of tuberculosis of the skin. I feel that the syphilitic infection may predispose to the development of a focus of tuberculosis and to the spreading of the disease in the body. If the eruption in the patient presented today is tuberculous, the marked extension in the comparatively short time would be explained by the syphilitic infection. I am eager to hear whether any of the members can tell me about the development of tuberculosis of the skin during a syphilitic infection.

Dr. H. C. Saunders: I simply wish to repeat that inoculations of animals and further studies will be made. In response to the question as to when these lesions developed, I wish to state that the treatment had not been interrupted at all. The treatment was started almost as soon as the second eruption developed, and the present lesions appeared while the patient was still receiving active treatment. It was because of the fact that they did develop at this stage of syphilis that I was led to the conclusion to which many others in the clinic agreed that they were due to tuberculosis. After further studies have been made I shall report the results.

Syringoma. Presented by Dr. Herman Sharlit.

J. A., a woman, aged 25, is presented from the clinic for cutaneous diseases of the Beth Israel Hospital. The lesions have been present since childhood and are profuse about the neck and axillae. The patient presents innumerable discrete, confluent, shiny, cystic papules the size of the point of a pencil. There are no symptoms associated with the eruption. The histologic diagnosis is syringoma.

DISCUSSION

Dr. E. William Abramowitz: Has the patient received any treatment?

Dr. Herman Sharlit: Yes. She apparently received some local therapy which produced a dermatitis. Aside from that there has been no treatment.

Dr. J. A. Tolmach: The histologic section of one of the lesions in this case showed the presence of several epithelial cords in some of which were seen cysts which contained some amorphous material. There was, too, a much enlarged sebaceous gland. The picture was that of syringoma, but it is interesting to note that interspersed among the syringomas were many superficial cystic lesions; from one of these a typical milium was expressed.

Dr. E. William Abramowitz: From the standpoint of treatment I think it would be proper to mention that in a similar case I employed roentgen therapy. The lesions became almost inconspicuous and in certain areas seemed to have disappeared after administration of about twelve weeks of ¼ units (75 roentgens) of unfiltered roentgen rays. There are a few reports of similar occurrences in the literature.

Dr. Herman Sharlit: I think that the suggestion made by Dr. Abramowitz is a good one. Probably roentgen irradiation will cause atrophy in the parenchymatous tissue and improve the appearance of the lesions.

A Case for Diagnosis (Impetigo Contagiosa?). Presented by Dr. Henry D. Niles.

R. D., a white girl aged 10 years, was first seen this afternoon at the clinic for cutaneous diseases of the New York Hospital. One year ago, in August 1933, the child was at the Willard Parker Hospital for sixteen days with anterior poliomyelitis, the sequela of which is a slight weakness of the left leg. She was vaccinated at the Willard Parker Hospital one year ago. The present condition began ten days ago and is asymptomatic. The general health is unaffected by the presence of the lesions. She presents a bilateral, roughly symmetrical eruption on both buttocks, consisting of discrete, crusted, ulcerated areas from the size of a dime to that of a half-dollar, each surrounded by a narrow zone of scarlet erythema. The largest lesion is on the right buttock; its appearance preceded that of the others by about twenty-four hours. There is no induration around the lesions. There are a few new pinhead-sized pustules.

DISCUSSION

Dr. Edward R. Maloney: This case impresses me as one of ecthyma. If there were a history of ingestion of bromide I should consider the possibility of bromoderma. Without that history I think the eruption is ecthyma.

Dr. Sigmund Pollitzer: To me the condition appears to be a simple impetiginous infection. I do not see anything in the eruption suggestive of ecthyma. In ecthyma there is ulceration. There is no ulceration in this case. The epidermis is not destroyed in any of the lesions except superficially. I believe the patient has simple impetigo contagiosa.

Dr. A. Benson Cannon: I think the lesions are superficial, excoriated and show hemorrhagic crusting but no sign of being infected. I am of the opinion that they are self inflicted, probably from picking with the finger-nails.

Dr. Max Scheer: I agree with the diagnosis of ecthyma or deep impetigo.

Dr. Isadore Rosen: I cannot understand the diagnosis of ecthyma in a case like this. Those of the members who see cases of this nature, and most of them do, would not hesitate if they saw this eruption on the face to make a diagnosis of impetigo. I think it is an ordinary case of bullous impetigo contagiosa, in which the bullae rapidly rupture and the eruption takes on a somewhat different form, perhaps on account of the location. Usually one sees impetigo on the face, chest and neck. Ecthyma consists of deep, ulcerative, pyogenic lesions, while this patient's lesions are superficial. I dare say that the use of soap, water and a mild antiseptic, with instructions to the patient regarding precautions against the spread of the condition, will be followed by a cure within a week. But I object to the diagnosis of ecthyma.

Dr. Max Scheer: Certainly if these lesions were seen on the face one would hesitate to call them ordinary impetigo contagiosa. There are no honey-colored, stuck-on crusts, and the lesions are not superficial. There is no telling how deep or shallow the ulcers are until the crusts are removed. The impression from the lesions with the inflammatory halo around them is that there is some ulceration under the crusts. In ecthyma the depth of the ulceration is variable according to the resistance of the tissues and so on. I am convinced that this eruption is not a straightforward impetigo contagiosa.

Dr. Eugene F. Traub: One thing is certain about this case. The patient presents several clear, small vesicles with practically no inflammatory base. Therefore, the condition undoubtedly began as a vesicular or bullous eruption. Impetigo is by far the most likely diagnosis.

Dr. Marion B. Sulzberger: In reply to Dr. Scheer's statement, I wish to say that I took off one of the crusts and there is no ulceration underneath.

Dr. Henry D. Niles: I wish to apologize for presenting this patient, as I know so little about her. I saw her as I was about to leave the clinic today. The only reason for presenting her is the unusual distribution of the lesions.

The first impression suggested the possibility of bilateral herpes zoster, although I know that such a condition occurs extremely rarely, if ever. I do not think that the condition can be regarded as a simple impetigo. The distribution of the lesions argues against impetigo, in which the lesions are of the "hit or miss" distribution. The arrangement of this patient's lesions is definitely linear. In addition to that, she has a neurologic condition, and that may have unduly influenced the members' opinion. She has had poliomyelitis. I certainly agree that the most likely diagnosis is impetigo contagiosa, but I do not agree that it is an ordinary case.

DR. ISADORE ROSEN: There is one point I am glad that Dr. Niles brought up, namely that while it was thought at first the condition might possibly be herpes zoster, it is now believed to be impetigo contagiosa. Ecthyma does not develop within a few days. The facts that all these lesions developed within a few days and that herpes zoster was considered do, I believe, justify the diagnosis of impetigo contagiosa.

DR. MAX SCHEER: The etiologic agent is a micro-organism, some form of streptococcus. Whether the infection is superficial or deep depends a great deal on the local resistance. In some persons, and particularly on the lower extremities, the resistance is lower, and the reaction of the streptococcus, instead of being exceedingly superficial as in ordinary impetigo contagiosa of the face, is more severe. There is more destruction of tissue, as occurs sometimes in run-down and alcoholic persons.

DR. EDWARD R. MALONEY: Since I started this discussion, I want to endorse all that Dr. Scheer has just said and also what he said before.

LUPUS VULGARIS (REPORT OF A CURE). Presented by DR. EUGENE F. TRAUB.

B. K., a woman aged 28, born in Russia, is presented from the Stuyvesant Square Hospital. The lupus was first noticed on the right ear when the patient was 2 years of age. At the time I first saw her, in September 1929, the entire lobe of the ear, which was large and pendulous, was made up of lupus tissue. There was some involvement of the skin just anterior to the ear. Between September 1929 and October 1932 the patient received eight roentgen treatments, and the lobe of the ear was removed with a cutting current of the endotherm knife. Some of the superficial patches that failed to respond to other therapy were painted with trichloracetic acid. Examination of a biopsy specimen as well as of the tissue removed at the time of the operation confirmed the diagnosis of lupus vulgaris. The patient has been free from the eruption since October 1932.

The reasons for presenting her are as follows: 1. At the last meeting of this section, a patient with an exactly similar condition was presented, and a request for therapeutic suggestions was made. 2. The method employed in the treatment of this patient is simple and effective, and the cosmetic result is good. 3. The patient has remained well for more than two years.

DISCUSSION

DR. MAX SCHEER: I think this is the best result I have ever seen in such a case.

DR. MARION B. SULZBERGER: First I wish to say that the result is good, and Dr. Traub is certainly to be complimented on achieving it. One frequently hears people say that an eruption cannot be lupus vulgaris because it has lasted for twenty years or more without any signs of growth or destruction of tissue. I have seen cases of lupus vulgaris which started in infancy or early childhood, so early that the patients and their relatives said that the lesions were birthmarks. The condition may remain unchanged for from fifteen to twenty years. This is a particular form which remains stationary and starts when the patient is very young; the involvement may be single or multiple.

DR. ANTHONY CIPOLLARO: The patient presented here last month by Dr. Rosen with a diagnosis of lupus vulgaris had had the lesion, I think, for twenty-seven

years. The lesion on the lobe of the ear was thought to be a keloid. It was excised about two years ago. After the surgical intervention the lesion recurred and seemed to grow more rapidly. That patient presented an example of a type of lesion which recurred after complete surgical removal and remained localized for twenty-seven years.

PERIADENITIS MUCOSA NECROTICANS RECURRENS. Presented by DR. HERMANN FEIT.

S. N., a Jewish man aged 39, a piano tuner, is presented from the department for cutaneous diseases of the Vanderbilt Clinic because of an eruption in the mouth of four years' duration. There is an uncertain past history of syphilis, and the Wassermann reaction is said to have been positive. For the past four years the patient has had recurrent ulcers on the mucous membrane of the lips, tongue, cheeks and gums. Each lesion lasts about three months and heals with or without treatment. The lesions are painful, and they have prevented the patient from working. The tonsils, adenoids and all the teeth except four of the lower ones have been removed on account of these lesions. Examination shows on the right upper lip a round ulcer, 1.5 cm. in diameter, forming almost a hemispheric depression. There is no undermining or induration. There is a small superficial ulcer on the left upper gum. There are also a healing ulcer on the back of the tongue, a small lesion on the frenulum and a wound on the right cheek near the alveolar ridge caused by removal of tissue for biopsy. There is no adenopathy.

The Wassermann reaction was negative. Smears failed to show the tubercle bacillus, Vincent's organism or Bacillus crassus. The results of a test meal showed: free hydrochloric acid, 56; total acidity, 86. The test with tuberculin (1:10,000) was negative. A biopsy specimen showed chronic inflammation.

DISCUSSION

DR. CHARLES WOLF: These chronic ulcerations are stubborn and resistant to treatment. Hoffman has recently described a series of conditions and given them the name of chancriform pyoderma. Ulcus vulvae chronicum is included. He claims that they are due to a streptococcus and that they are a highly resistant type of infection.

DR. T. J. RIORDAN: During the past two years in Dr. Maloney's service at St. Vincent's Hospital my co-workers and I have seen several cases of this malady. The peculiar feature in this case is the absence of lesions on the tongue. In the cases we saw the condition started as painful lesions on the tongue which broke down. We found that the lesions responded to treatment with a 50 per cent solution of glycerite of boroglycerin and to roentgen therapy.

DR. SIGMUND POLLITZER: About twenty-five years ago Dr. Sutton called on me to show me some slides demonstrating pathologic reactions in a disease he was studying. He wanted to know if I did not think the disease was a form of a condition I had described some years before under the name of hidradenitis suppurativa, which is now known as papulonecrotic tuberculid. It certainly had a strong resemblance to it. There was a lesion in the region of one of the mucous glands instead of around a coil of a sweat gland. I think that since that time, though many cases have been seen and studied, nothing, either in the way of clearing up the etiology or in making suggestions for therapy, has been added to what Dr. Sutton wrote.

DR. DAVID BLOOM: Dr. Feit remarked that this is a rare condition. I have seen a number of cases. The disease is always highly resistant. The main difficulty, however, consists in preventing a recurrence.

DR. HERMANN FEIT: The malady may not be as rare as it is thought to be. At Professor Weibl's gynecological clinic in Vienna I saw several women who had similar lesions on the labia pudendi. Bacillus crassus was not found. It is known that aphthous ulcers may sometimes appear on the labia.

DR. SIGMUND POLLITZER: In reference to stomatitis aphthosa, the disease of Sutton begins under the surface, while stomatitis aphthosa is a superficial infection which may penetrate more or less deeply but always begins on the surface. On the other hand, Sutton's disease begins under the surface like a tuberculid. The patient can palpate with his tongue a little lump under the surface. After a while the infiltration comes to the surface, and ulceration follows. The course of the lesion in this case excludes stomatitis aphthosa.

DR. HERMANN FEIT: It was for the reasons just given by Dr. Pollitzer that I doubted that these two conditions were the same, but Dr. Sutton in his textbook gave the two titles as synonymous. The disease is supposed to start with submucous nodules. I cannot conceive of this being true in aphthous stomatitis.

GRANULOMA ANNULARE. Presented by DR. HERMANN FEIT.

G., a man aged 46, an accountant born in the United States of French parentage, is presented because of lesions on the left upper eyelid and left cheek of one year's duration. He has always been in good health. There is no history of tuberculosis in the family. He is a fairly heavy smoker. For the past seven years he has had seborrhea. About eighteen months ago, while he was receiving treatment for seborrhea, a doughy swelling about the size of a small lima bean developed at the inner canthus of the left eye. The surface was oozing at times. This tumor practically disappeared under fractional roentgen treatment with 75 roentgens once a week which was given for the seborrhea. There was a recurrence because the patient did not present himself for treatment for about six months.

About three months ago, after a sojourn in Canada, the patient returned for treatment, and it was observed that an oval infiltration which nearly covered the whole left upper eyelid had developed. The skin over this area is normal and not discolored. There are no pearly or papular lesions. The eyelid is swollen so that only half of the aperture can be seen. There is no pain or any other sensation. At a distance of about 2 fingerbreadths in front of the left ear is an annular infiltration approximately 1 inch (2.5 cm.) in diameter which shows, on stretching, a definite papular border.

The Wassermann reaction and the test with tuberculin (1:10,000) were negative. The biopsy report was as follows: "The histologic diagnosis was granuloma annulare. The sections showed a marked granulomatous change which surrounded edematous follicles with degenerated epithelium. Numerous eosinophils and large mononuclear cells which resembled epithelioid cells were seen. Numerous lymphocytes were seen. The voluntary muscle fibers were invaded. Beneath the thin surface epidermis was seen a cystic comedo filled with keratin. This may have been the source of the inflammatory manifestation. I think that the hemoblastic concept of the etiology of this condition must be given minor consideration.

DISCUSSION

DR. G. F. MACHACEK: The histologic picture is not characteristic of granuloma annulare. The disease may be mycosis fungoides. One must remember that in this particular section there were included cysts full of keratin, and there was a secondary inflammatory process which probably tended to mask the primary histologic changes. I do not think that one can rule out mycosis fungoides, and I do not think that one can rule out granuloma annulare on the basis of the histologic picture. However, I will say that the characteristic little nodules one sees in granuloma annulare, with central necrosis and a zone of epithelial cells and leukocytes, are not found. I think all the members will realize the difficulty of making a differential diagnosis between granuloma annulare and mycosis fungoides, particularly when the follicles are inflamed and infiltrated with polymorphonuclear leukocytes.

NOTE.—After seeing the case I feel obliged to change the diagnosis to granuloma annulare.

DR. HERMANN FEIT: I think this is one of the most puzzling cases my co-workers and I have ever seen. This patient has been under treatment for

several years for so-called seborrhea. About eighteen months ago he had a tumefaction of the eyelid about the size of a quarter from which serum was secreted. We were much puzzled and were unable to make a diagnosis. We applied no treatment and watched to see what would develop. When the patient returned six months ago the tumefaction had completely disappeared, and a complete ring had formed around the upper eyelid, the ring of course being more ovoid to conform to the anatomic structure of the lid. On examination no papular or nodular formation is seen. The ring has the ivory color seen in granuloma annulare. On examining the left cheek, where seborrhea had been present, we saw nodules, set in a circle, when the skin was stretched. These nodules are not present tonight because roentgen therapy has been administered. On closer examination tonight it could be seen that the so-called seborrheic patches were definitely infiltrated. Therefore there still is a doubt as to whether the disease is really granuloma annulare or an early stage of mycosis fungoides. As for the histologic picture, sections are presented, and Dr. Machacek can give the details. However, in describing the condition to me he felt that it might fit in with either one or the other diagnosis and that therefore histologically a definite conclusion cannot be reached. The tuberculin test was negative. While in granuloma annulare that test is supposed to be positive, there have been other cases in which it was negative at first and became positive a few months later.

DERMATITIS HERPETIFORMIS; MARKED IMPROVEMENT AFTER MEDICATION WITH CHROMIUM SULPHATE. Presented by DR. E. WILLIAM ABRAMOWITZ.

M. P., a boy aged 6 years, was presented at the meeting of the American Dermatological Association in June 1934 as having a classic eruption of dermatitis herpetiformis of one year's duration (the report of the presentation did not appear in the transactions as published in the ARCHIVES of December 1934). He was treated with injections of his own blood but failed to improve. In September he was given 1 grain (0.06 Gm.) of chromium sulphate by mouth, three times daily. About two weeks later he began to improve. During the past month he has been receiving cod liver oil. The remaining lesions at this time are located on the right knee and right elbow. The accompanying photographs show that there has been considerable improvement since he has followed this form of treatment.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: After the patient was presented in June, it was decided to give him hemotherapy. There was practically no influence on the eruption. I later read of the use of chromium sulphate in dermatitis herpetiformis in the transactions of the Philadelphia Dermatological Society (ARCH. DERMAT. & SYPH. **30**:128 and 131 [July] 1934). One patient with dermatitis herpetiformis was presented by Dr. Weidman and Dr. Gilman, and another was presented by Dr. Cormia for Dr. Stokes. In the case of Dr. Weidman and Dr. Gilman it was reported that immediate regression of the lesions had followed the use of chromium sulphate, a form of treatment suggested by Dr. Roussel of New Orleans. In the discussion on Dr. Cormia's case Dr. Guequierre stated that he had obtained good results from treatment with chromium sulphate. The dosage for adults is 4 grains (0.26 Gm.) three times daily, in capsule form. I asked Dr. Gilman for more information, but he does not want to commit himself as the number of cases in which this treatment has been used is too small to permit any conclusion. I gave this patient 1 grain of chromium sulphate in water, after the urine had been examined, because it is said that chromium sulphate irritates the kidneys. I did not see much improvement in the first three or four weeks, but since then the improvement has been rather marked. The patient has two lesions now as compared with the numerous lesions he had during the summer. He is also taking cod liver oil. As far as I know, cod liver oil has no effect on dermatitis herpetiformis.

The basis for this treatment has not been mentioned. It seems that chromium sulphate was used in 1902 and in 1908 for neurasthenia, tabes and other nervous conditions, but no adequate confirmation of these observations can be found.

This boy's urine has been examined weekly, and so far 1 grain of chromium sulphate three times a day after meals has not caused any renal irritation. This treatment has therefore been continued, and I hope that the members will get interested and see what effects they observe with its use in similar cases. Of course, it is known that cases of dermatitis herpetiformis have been reported in which the condition was benefited by various methods of treatment. It is therefore difficult to draw any definite conclusions, but I think this remedy should be given a trial with proper control to see whether it has any definite value in the treatment of this stubborn disorder.

DR. EUGENE F. TRAUB: I wish to endorse Dr. Abramowitz' statement about being careful in drawing conclusions. This disease has remissions. The improvement in this case may be merely a remission, but I hope that this is not true, as there is much need for an effective drug for dermatitis herpetiformis.

DR. J. A. TOLMACH: Chromium sulphate irritates the kidneys and because of this its value should be carefully ascertained before its general use is advocated. It is difficult to evaluate a remedy properly in a disease which is known to have spontaneous remissions. At the Beth Israel Hospital there is a patient with an old, recurrent case of dermatitis herpetiformis. The itching was severe, and the patient obtained no relief from the usual remedies. At the suggestion of Dr. Sharlit this patient was given injections of a solution which Dr. Sharlit had prepared and with which he has had good results in relieving pruritus in cases of dermatitis venenata. This treatment in this case was not particularly rational and could at best be considered a form of nonspecific therapy. At any rate, the pruritus was almost immediately relieved, and, more remarkably, the lesions began to resolve. It is certainly difficult to state whether or not this good result was a coincidence. Dr. Sharlit will probably be glad to tell the members more about the nature of this solution.

DR. HERMAN SHARLIT: I cannot at this time intelligently report on the nature of the material used.

CHRONIC ULCERATIVE PYODERMA. Presented by DR. DAVID BLOOM.

Mrs. T. F., a Jewish-American housewife aged 40, is presented from the service of Dr. Abramowitz at the Jewish Memorial Hospital because of an eruption of four years' duration. She was previously presented at the meeting of this section in October 1932 and again in December 1932 (ARCH. DERMAT. & SYPH. **27**:693 [April]; 869 [May] 1933).

DISCUSSION

DR. DAVID BLOOM: At the two previous presentations (October and December 1932) I reported the history of the case and the results of the laboratory examinations. All other diagnoses could be excluded and the conclusion was reached that the eruption was due to the effect of staphylococci in a person of low resistance. I am presenting this patient tonight to show the scars of the healed lesions. Since the last presentation the patient has had several recurrences of bluish discoloration and breaking down of the skin on the outer side of the left ankle. This was associated with an exacerbation of colitis. The treatment has consisted in raising the general condition of the patient by administration of liver extract, iron, arsenic and ultraviolet radiation. At times small doses of roentgen rays were used.

ECTODERMAL DEFECT. Presented by DR. HERMAN GOODMAN.

R. G., a girl aged 2½ years, is presented from the Stuyvesant Square Hospital. There is a loss of hair over part of the scalp (the periphery), with a noninflammatory reaction. There are no eyelashes or eyebrows. Scant hair, thin and light blond, is present on the top of the scalp. All the nails show defective growth. The mother of the patient states that the condition has been present since birth and that no change has been noted. Various examinations, including study of the blood and of the sella turcica, have been made, but no results are available at present.

R. H. RULISON, M.D., *Chairman*

Dec. 4, 1934

E. WILLIAM ABRAMOWITZ, M.D., *Secretary*

BOECK'S SARCOID (LUPOID)? ANGIOLUPOID? Presented by DR. FRANK VERO.

F. T., a girl aged 5 years, born in the United States of Greek parentage, is presented from the pediatric service of St. Vincent's Hospital. She was first seen about six months ago. The parents stated that in November 1933 they noticed a small reddish spot on the child's chin; this gradually grew larger, and several new spots appeared in the same area. There is no history of any previous cutaneous disease. The child has had measles, mumps and whooping cough. The parents and seven brothers and sisters are alive and well.

Physical examination gave negative results. On the right side of the chin there are numerous lichenoid, papular lesions and a larger plaque, which are grouped in an almost linear distribution. The larger plaque was the first lesion. It measures approximately 1.5 by 0.75 cm. and is irregularly shaped, elevated from 2 to 3 mm., sharply defined, yellowish-red, markedly infiltrated and slightly firm. A few fine areas of telangiectasia are visible on the periphery of the lesion. The surface is shiny, stretched and uneven as though the lesion consisted of the conglomeration of numerous smaller nodules. The epithelium is unaltered. Close by there are three similar papular lesions varying from the size of a pea to that of a bean but less raised and infiltrated than the large plaque. Five isolated pinhead-sized, yellow-brownish, lichenoid lesions, scarcely raised above the surface of the skin are seen extending upward. The examination with the diascope showed a diffuse light yellowish discoloration and two or three grayish puncta on the border of the largest lesion.

The Wassermann and Kahn reactions were negative. Examination of the blood showed 5,600,000 red cells and 5,500 white cells, 42 per cent of which were polymorphonuclear leukocytes, 46 per cent lymphocytes, 2 per cent mononuclears and 10 per cent eosinophils. The hemoglobin was 60 per cent; there were marked achromia, moderate polychromatosis and basophilic stippling. Roentgen examination of the chest and long bones disclosed no abnormalities. Tuberculin tests with Mantoux (1:1,000), bovine and avian tuberculin all were negative.

The biopsy was reported to show tuberculid. The treatment has consisted of oral administration of solution of potassium arsenite and ultraviolet irradiation from the air-cooled quartz mercury vapor arc lamp. The lesions on the chin have become somewhat flatter and softer. The small lichenoid lesions have remained unchanged. No new lesions have appeared during the past six months.

DISCUSSION

DR. SIGMUND POLLITZER: Whatever the clinical appearance of the lesions, the histologic examination should be absolutely determinative. If the structure is tuberculoid, the condition is obviously not a simple hemangioma. I do not know who made the histologic examination, but perhaps the pathologist would be willing to furnish a report on it. That is really the crucial point in making the diagnosis.

DR. DAVID L. SATENSTEIN: I agree with what Dr. Pollitzer has just said. I do not understand what was meant by tuberculid. I have seen many different pictures in tuberculid, and it appears necessary to have the pathologist describe what he found.

DR. T. J. RIORDAN: I saw this patient at St. Vincent's Hospital, and I also saw the sections. Dr. Alexander Fraser examined the tissue. As I remember this tissue, it showed a tuberculoid structure, that is, an infiltration consisting of epithelioid cells and round cells showing a high percentage of epithelioid cells.

DR. FRANK VERO: When I saw this patient for the first time I thought that possibly the condition was a hemangioma, but there were four or five pinhead-sized lichenoid lesions which did not fit into the clinical picture of hemangioma. This made me change the diagnosis. The course and the clinical appearance of the lesions suggested some type of tuberculoderma. Close observation of the large plaque showed that it was composed of numerous small nodular lesions, but on examination with the diascope no apple jelly nodules were visible; there was only a diffuse light yellowish discoloration. One of the lesions was excised, and one half of the tissue was used for a biopsy; the other half was used for inoculation of animals. The result of the inoculation was negative. The biopsy report (as given by Dr. Alexander Fraser) was: "Tuberculid." A diagnosis of sarcoid was then considered, although that condition is rare in children. I looked up the literature on sarcoids and found that, according to Martenstein, up to 1924 only two cases had been observed in children below the age of 10 years, and these two cases occurred in children below 5 years of age. The occurrence of sarcoid in children and in infants has been reported since by Leidi, Tuerk, Gottron and others. All the authors who have studied the subject remark that the cases are not as characteristic in children as in adults, owing to the peculiar reactivity in children. The color in this patient's lesions is suggestive of angiolupoid. I have never seen such a case but I have read on the subject. The appearance does fit in somewhat with the description given by Brocq and Pautrier, although the color in the case described was somewhat blue. In most of the cases reported the lesions were located on the nose and cheeks. As to the etiology of angiolupoid, most authors believe it to be tuberculous. In this case the negative tuberculin test and the clinical course lead me to believe that the condition is angiolupoid.

ADENOCARCINOMA. Presented by DR. ISADORE ROSEN.

M. S., a woman aged 55, was born in the United States. She has three children and has had no miscarriages. She was first seen in the clinic for cutaneous diseases of the New York Post-Graduate Medical School and Hospital on Nov. 19, 1934, at which time she stated that she had a tumor of the roof of the mouth, which had been present for twenty-four years. She says that the lesion started soon after she had a tooth extracted, and she has been advised by several physicians to leave it unmolested. It has been steadily growing in size. About three months ago she noticed that the surface of the tumor began to look "raw" and "to bleed." At present this patient presents on the left side of the soft palate a tumor measuring 5 by 7 by 2 cm. It is pinkish and firm but not cartilaginous. The surface is eroded. The patient is in good general health, and there is no pain or discomfort of any nature. There are no palpable glands, and there has been no loss of weight recently.

Microscopic examination revealed an adenocarcinoma of the salivary gland type with squamous cell metaplasia.

DISCUSSION

DR. ADOLPH ROSTENBERG: I suggest the diagnosis of epulis, although tumors of that type grow more rapidly and are more malignant than appears to be the case with this patient's lesion.

DR. ANTHONY CIPOLLARO: The patient first noticed this lesion about twenty-five years ago, after undergoing extraction of a tooth. It gradually grew in size until about four months ago when the surface started to become slightly eroded. A part of the erosion is the result of excision of tissue for a biopsy about three weeks ago. The lesion has grown steadily in size and has never annoyed the patient in any way. There has been no opportunity to work up this case, as the patient has been seen only twice. A biopsy was made at St. Peter's Hospital, New Brunswick, N. J., and I understand that a diagnosis of mixed cell tumor was made. That information was obtained by telephone. Roentgen examination does not show an actual extension of the tumor to the left antrum. There are no palpable nodes. There has been no loss of weight recently. The patient is well nourished, and the

tumor does not appear to interfere with her well-being. The Wassermann and Kahn reactions have been negative. From the clinical findings, one can say that the patient has a benign tumor of long standing, the nature of which has not been determined. The case will be thoroughly studied before therapy is instituted.

INFECTIOUS ECZEMATOID DERMATITIS. Presented by DR. E. WILLIAM ABRAMOWITZ.

T. P., a woman, aged 21, was first seen at the department of dermatology and syphilis of the New York Post-Graduate Medical School and Hospital two years ago with a profuse vaginal discharge of a few years' duration, a marked crusted and pustular eruption of the scalp and pustular, follicular lesions affecting particularly the axillae and pubic region. Since that time the patient has been under the care of the gynecological department, and the condition has been reported as "suggestive of infestation with Trichomonas." Bacteriologic examination of pus showed Streptococcus haemolyticus. Treatment consisting of irrigations with various antiseptics is being given at the gynecological department.

At present the scalp is clean, and most of the lesions on the body have disappeared. There are eczematous patches in the axillae and follicular lesions on the back and groins.

DISCUSSION

DR. FRED WISE: I wish to call attention to the fact that this woman had lesions on the eyebrows and on the glabella resembling seborrheic dermatitis.

DR. LOUIS CHARGIN: The fact that the eruption appeared first behind the ears and in the axillae and the groins points to the diagnosis of seborrheic eczema rather than to that of infectious eczematoid dermatitis. The history of focal infection generally associated with the latter seems to be absent in this case.

DR. E. WILLIAM ABRAMOWITZ: About two years ago this patient had an impetiginous eruption on the scalp and ears, a definite pustular eruption on the face, numerous pea-sized pustular lesions on the entire trunk and a weeping, pustular, eczematous eruption in the axillae and on the entire vulvar region. A profuse vaginal discharge preceded the cutaneous eruption. The condition at that time showed no resemblance to seborrheic dermatitis. The patient was treated with baths of permanganate and local applications of silver nitrate and antiseptic ointments to the weeping eczematous areas. She was also treated at the department of gynecology where at one time Trichomonas vaginalis was found. Bacillus coli, staphylococci and streptococci were found in the vaginal smear. The patient has improved considerably, but she still has a profuse definitely pustular eruption on the vulvar area and a profuse vaginal discharge. The reason for presenting her as having infectious eczematoid dermatitis is that she had a primary focus, a discharge from the vagina and outbreaks of pustular lesions which recurred up to about a year ago and occur even now but to a much less extent than when she was admitted. The vulvar lesions and the weeping lesions in the axilla seem to be obstinate and do not respond to any form of treatment that has been tried so far.

PSORIASIS? Presented by DR. V. A. H. CORNELL.

E. D., a boy aged 9 years, has had lesions involving the nails of the right index finger and right and left thumbs for two years. He was first seen at the department of dermatology and syphilology of the New York Post-Graduate Medical School and Hospital on Nov. 26, 1934, at which time examination showed the right index finger-nail and the nail of the right thumb to be irregular, hypertrophic, deformed and discolored and covered with heaped-up crusts. The nail was thickened, and considerable paronychia was present. The nail of the left thumb was discolored, yellowish and pitted. On the left thumb there was some extension downward of a sharply defined patch composed of some vesiculation and maceration. The examination for tinea gave negative results.

DISCUSSION

DR. DAVID BLOOM: I agree with the diagnosis of psoriasis. The condition in this patient is of an exudative type. Cases such as this have been described frequently under the name of acrodermatitis continua of Hallopeau, but I believe that most of the cases described under this name in the literature belong in the group of exudative type of psoriasis, particularly in the group of pustular psoriasis.

DR. LOUIS CHARGIN: I accept the diagnosis of psoriasis. I do not think that the condition is acrodermatitis continua of Hallopeau. In that disease the primary lesion is vesiculopustular. The lesions develop on the skin around the nails, and only later do the nails become affected. Other parts of the skin, especially the hands, become affected with an exudative process, often with undermining of the skin. On the other hand, the type of psoriasis exhibited by this patient begins under the nails and may be limited to them, but often the usual type of psoriasis affects the adjacent skin.

DR. FRED WISE: How can this condition be differentiated from Hallopeau's disease?

DR. LOUIS CHARGIN: In Hallopeau's disease, the primary lesion is a vesicular pustule, and the process is moist by contrast. In this type of psoriasis the nail is dry.

DR. MARION B. SULZBERGER: While I am inclined to share the opinion that the picture presented by this patient is more like that of psoriasis than like that of acrodermatitis continua of Hallopeau, there is a history that in the beginning the lesion was nothing but an agglomeration of pustules. I believe that in this case it is impossible to make a differential diagnosis between acrodermatitis continua of Hallopeau and the pustular type of psoriasis until more information is obtained. I have found that in both diseases the lesions are sterile. Professor Jadassohn agreed with me that in both conditions the pustules are sterile if they are properly opened. I do not know whether the two diseases are the same. I know only that I cannot make a differential diagnosis in this case.

DR. SIGMUND POLLITZER: In Hallopeau's disease the process extends by an undermining of the epidermis with pus. That is characteristic of the disease which Hallopeau described about forty years ago. As to the diagnosis of psoriasis in this case, I must say that I see nothing in these lesions that is suggestive of psoriasis. Nevertheless, I should accept the diagnosis of psoriasis if in the future a definite, unmistakable lesion of psoriasis develops elsewhere on the patient's body. Until then I should leave the diagnosis of psoriasis with a large question mark. In fact, I should not accept the diagnosis.

DR. DAVID L. SATENSTEIN: I have had an opportunity to study quite a number of these cases of so-called pustular psoriasis. I have seen all of Dr. Andrews' specimens and many of Dr. MacKee's, and my co-workers and I have a large collection. As I stated before, from the pathologic changes I cannot see anything suggestive of psoriasis. Pustular psoriasis was described by Unna in 1890 under the name of chronic eczema with a sudden development of vesicular pustules. He gives one of the best descriptions I have ever seen of the picture found in cases of so-called pustular psoriasis. As I said before, microscopically the lesions show no feature suggestive of psoriasis, and the clinical course in these cases is certainly not that of psoriasis. I believe that the condition is a dermatitis with secondary eczema.

DR. V. A. H. CORNELL: This condition has been present on the two or three fingers affected for the past two years, and the patient's mother states that the lesions always began as scales underneath the nails and then extended around and below the nails. The lesions are sharply defined. The child came to the clinic about a week ago, and at that time the scales were piled up, white and thick. An ointment was prescribed in the clinic, and the appearance is somewhat different tonight from what it was when the patient was first seen last week.

DR. T. J. RIORDAN: As I have mentioned before, the cases of pustular psoriasis or psoriasis with pustules that I have seen certainly showed the features of psoriasis. Those features consisted of parakeratosis or hyperkeratosis, a decrease in or absence

of the granular layer, acanthosis and spongiosis and clubbing and fusion of the pegs. There was a decrease in the suprapapillary rete; that is, the papillae rose high. There were ordinary inflammatory changes in the corium. Along with these changes there was evidence of spaces between the region of the granular layer and the corneous layer; these spaces either were microscopically small, so-called Munro abscesses, or appeared as an agglomeration of those abscesses to form a pustule. Certainly those cases were cases of psoriasis, even without the agglomeration of abscesses.

DR. DAVID L. SATENSTEIN: I am sorry to say that if his description of the microscopic changes in those cases is correct, then Dr. Riordan has not seen any cases of so-called pustular psoriasis.

DR. T. J. RIORDAN: That is all true, and in the cases of Dr. Andrews and his co-workers (Andrews, G. C.; Birkman, F. W., and Kelly, R. J.: Recalcitrant Pustular Eruptions of the Palms and Soles, ARCH. DERMAT & SYPH. **29**:548 [April] 1934) the picture is such as I described, but in the patients who have been presented that picture is not true. The lesion is a pustule which appears clinically either as a vesicle with a translucent fluid in it or as a pustule. The agglomeration of the so-called abscesses was found at the corneous layer, not where Dr. Satenstein demonstrated. I agree with the statement that spongiosis and formation of vesicles in the rete may be due to eczema, but in the cases diagnosed as instances of psoriasis the pustules are not in the rete but in the corneous layer.

DR. DAVID BLOOM: Of the seven cases of pustular psoriasis of the palms and soles which my co-workers and I have observed, histologic examinations were made in four. In two of these cases the typical features of psoriasis which Dr. Riordan has mentioned were present. These cases demonstrated clearly the meaning of the pustules in psoriasis. In one case in which material for a biopsy was taken from the side of the foot all the features of psoriasis were not found, and the pathologist left the decision as to the diagnosis to the clinician. In the fourth case the histologic diagnosis was psoriasis with an intra-epidermal abscess. This abscess resembled the ones described in the aforementioned report of Dr. Andrews and his co-workers. It is quite possible that not all cases of pustular psoriasis of the palms and soles show a typical histologic picture of psoriasis. However, clinically, the morphology and course are so typical that no special diagnostic acumen is necessary to make the diagnosis after one or two cases have been seen and studied.

DR. PAUL GROSS: The discussion about the histologic picture is interesting but does not solve the problem. I wonder whether Dr. Satenstein and Dr. Riordan would agree on a diagnosis of lichen planus bullosus. After all, an exaggeration of the exudative process leads, on the one hand, to a lichen planus bullosus, and, on the other hand, to pustular psoriasis. I wish to apply this theory only to the fully recognized cases of pustular psoriasis reported in the older literature without taking a position in regard to the eruption on the palms and soles which has been so much discussed lately. Another important factor is the influence of the location on the histologic picture.

DR. FRED WISE: Regarding the clinical symptoms. I recently read an article by a German author, whose name I do not recall just now, who claimed that in his experience the differentiation between pustular psoriasis and Hallopeau's disease was this: In pustular psoriasis, at some time or other during the course of the disease, not necessarily when the patient is seen at a certain visit, as this patient is today, there will be seen small lakelets of pustules or pustulovesicles containing a milky fluid. The author stated that these little flaccid lakelets, as he called them, were characteristic of pustular psoriasis and that they did not occur in Hallopeau's disease. Whether that has any correlation with the histologic findings I cannot say. Whether his statement is true or not, I do not know. Few dermatologists see many of the cases which are called instances of typical pustular psoriasis. More or less guessing is necessary most of the time. I am inclined to agree with MacKee when he says that the only cases in which a clinical diagnosis can be made are those in which other evidences of psoriasis occur elsewhere on the body or in which there is a history of psoriasis on the knees, elbows, scalp or glans penis. It is difficult

to make a clinical diagnosis in a case such as this one. If the mother had stated that lesions of psoriasis were present elsewhere on the body or that such lesions occurred in other members of the family, that would undoubtedly lend support to the diagnosis.

DR. ISADORE ROSEN: I agree with the diagnosis as presented. This boy came in for the first time about a week or ten days ago with the lesions as shown tonight. Mycologic examinations gave negative results microscopically; the cultures have not been reported on as yet. The changes in the nails are typical of psoriasis. This patient was not presented as having pustular psoriasis, but as having psoriasis. In the clinics patients are frequently seen with palmar and plantar lesions on the basis of which a diagnosis of psoriasis can be made in spite of the fact that at the time no other evidence of the disease are present.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. E. WILLIAM ABRAMOWITZ.

M. S., a woman aged 59, was previously presented at a meeting of the Atlantic Dermatological Conference on Nov. 17, 1934, by Dr. MacKee, from the department of dermatology and syphilology of the New York Post-Graduate Medical School and Hospital.

The patient was first seen on Sept. 13, 1934, when it was stated that an eruption on the scalp, face, trunk, upper and lower extremities and dorsal and palmar surfaces of the hands had appeared after exposure to sunlight and had been present for one year. The eruption was violaceous, and in some places it was dry and red. It was slightly scaly. There were areas of atrophy, depigmentation and pigmentation. There were many areas of telangiectasia scattered over the involved areas. There was marked alopecia. Up to the present time the patient has received eight intramuscular injections of a preparation of bismuth, and improvement has resulted. She was in the hospital from Sept. 10 to Oct. 1, 1934.

On Sept. 12, 1934, the blood count showed 3,570,000 red blood cells, 78 per cent hemoglobin, and 5,500 white blood cells, with 72 per cent polymorphonuclear leukocytes, 21 per cent small and large lymphocytes, 6 per cent monocytes and 1 per cent eosinophils. On Sept. 24, 1934, the blood count showed 3,720,000 red blood cells, 88 per cent hemoglobin, and 6,000 white blood cells, with 63 per cent polymorphonuclear leukocytes, 23 per cent lymphocytes, 7 per cent monocytes, 6 per cent eosinophils and 1 per cent basophils.

On Sept. 24, 1934, the result of a biopsy was reported as "histologic changes of a toxic nature." Again on Oct. 1, 1934, the same report on the biopsy was given.

DISCUSSION

DR. HERMANN GOLDENBERG: I agree with the diagnosis of lupus erythematosus disseminatus.

DR. HOWARD FOX: I agree with Dr. Goldenberg that the condition is most likely lupus erythematosus disseminatus, though the number of leukocytes was not as low as it usually is in this disease.

DR. ISADORE ROSEN: This patient was first seen at the New York Post-Graduate Medical School and Hospital two or three months ago. She was in a medical ward because of a generalized eruption which involved the scalp, face, chest, thighs and back. The eruption was primarily erythematous in character, and interspersed between the large erythematous patches were small islands that looked almost like atrophies. In fact some of the physicians who saw the patient before I did made a diagnosis of morphea or some form of scleroderma. The patient had lesions in the ears and a degree of alopecia such as is often seen associated with a generalized eruption. In my opinion the lesions on the hands gave a clue to the clinical diagnosis. Patients with lupus erythematosus have distinct lesions on the palms, and especially on the tips of the fingers, which are erythematous and scaly and present small areas of atrophy and telangiectasia. I was not certain of the diagnosis, but it was one of four or five that I considered.

An interesting feature of the case is that the patient is rapidly getting well under treatment consisting of intramuscular injections of a bismuth preparation. I think that the presenter should discuss this. Tonight she has a small number of active lesions as compared with the number she had when she was in the hospital. A biopsy did not substantiate the diagnosis of lupus erythematosus, but the condition was reported to be a toxic dermatitis.

DR. LOUIS CHARGIN: In recent years my co-workers and I have been seeing an increasing number of cases of this condition, especially just after the summer. Many of the patients give a history of a recent sunburn. The disease attacks the exposed parts of the face and chest and both aspects of the hands, but is more characteristic on the palmar aspect. The process is essentially an erythema with scaling and is either acute or subacute. It is frequently associated, but not necessarily so, with severe symptoms. The course may be short, but more often it is protracted, ending with death or with recovery. If recovery takes place the skin retains the usual atrophy seen in lupus erythematosus. Judged from the clinical standpoint the disorder appears to be a subvariety of lupus erythematosus and not a separate entity.

DR. HERMANN FEIT: About a week ago a pathologist gave a report on ten fatal cases of lupus erythematosus. I asked him if he had ever seen any cases starting with the clinical picture of the discoid type. Although he admitted that he was not well versed in dermatology, he informed me that he had never seen the hyperkeratoses and other changes that are observed in cases of lupus erythematosus. I think that an agreement should be reached as to what is really to be called lupus erythematosus. What is the clinical basis of this condition? Two different entities are being labeled lupus erythematosus. Sometimes in fatal cases a diagnosis of acute lupus erythematosus is made. The patients frequently have nephritis, and they have these erythematous lesions, but I have never seen any of these cases starting from what is called clinical lupus erythematosus. Also, does one ever see acute lupus erythematosus developing out of the discoid circumscribed type of lupus erythematosus? I brought a patient here tonight whose case may be of interest in connection with this subject. He states that he has been repeatedly subjected to direct exposure to sunlight for a number of weeks, as a result of which erythematous and hyperkeratotic lesions and atrophy have developed on the forehead. The interesting point I want to bring out is that in some patients sensitization to light seems to result from alimentary habits. For instance, the man whose case I mentioned states that he eats uncooked cereals every day. The disease may have some relation to the so-called buckwheat disease which occurs in animals, especially in sheep, I believe. I have reported a case that substantiates this theory.

DR. HERMANN GOLDENBERG: I think that some of the speakers tonight have confused two different diseases. When I accepted the diagnosis of lupus erythematosus I did not have in mind lupus erythematosus exanthematicus, the clinical picture of which is different from that of lupus erythematosus disseminatus.

DR. DAVID BLOOM: I saw an eruption of large erythematous plaques on the arms and trunk associated with typical lesions of lupus erythematosus on the face and scalp and a bullous lesion on the chest in a patient presented last week at a meeting of the Bronx Dermatological Society (ARCH. DERMAT. & SYPH. **31**:764 [May] 1935). I am impressed with the marked peculiar mottled pigmentation of some of the patches which I have observed in several cases, and I wonder whether this finding may not be of use in making a diagnosis.

DR. FRED WISE: I do not think that this patient has lupus erythematosus. I had the opportunity to study her lesions while she was in the wards of the New York Post-Graduate Medical School and Hospital. I believe that she presents the inflammatory and degenerative changes which precede the picture of lichenoid scleroderma and that in its later stages her eruption will resemble that condition, as pictured by Shelmire and me (Wise, F., and Shelmire, B.: Chronic Atrophic Lichenoid Dermatitis (Csillag); So-Called Lichen Albus of Zumbusch, ARCH. DERMAT. & SYPH. **18**:179 [Aug.] 1928).

Dr. E. William Abramowitz: My co-workers and I first saw this patient last September. Her temperature was from 99 to 100 F. at the most. Her pulse was not abnormal, and she did not seem to be acutely ill, but on account of the extent of the eruption we thought it wise to hospitalize her. She was transferred to the clinic after two weeks, as moderately improved. So far as I can recall there was no history of sensitivity to light or of sunburn. The eruption was unusual in our experience. Dr. Wise had seen the patient first, and he was definitely convinced that she had lichenoid sclerosed patches. Dr. Rosen and I saw her, and because of the diffuse erythema and the location we favored the diagnosis of generalized lupus erythematosus. We were much disappointed when in the first report of the biopsy the disorder was diagnosed as toxic erythema; the second report, given a week or so later, confirmed the histologic diagnosis of toxic erythema. In the meantime, we gave the patient injections of a bismuth preparation, and she began to improve immediately. The improvement consisted of subsidence of the erythema with subsequent pigmentation. At that time she had lesions on the hands too, but they were not as conspicuous as they are tonight. Certainly the lesions on the hands are characteristic of lupus erythematosus. I still favor the diagnosis of lupus erythematosus of the chronic generalized type, but I as yet am unable to account for the lichenoid patches.

Molluscum Contagiosum? Presented by Dr. Joseph L. Morse.

B. M., a girl aged 6 years, is presented from the New York Post-Graduate Medical School and Hospital because of an eruption on the face which began a year ago, new lesions continuing since then to appear on the face and trunk. The mother states that the child has not picked the lesions. There is no history of ingestion of drugs, but iodized salt has been used at various times.

On the face there are many erythematous, papular lesions of varying sizes, some of which are quite raised. There is no necrosis and no scarring from old lesions. There is no scaling or ulceration, and on pressure with the diascope no yellowish nodules can be seen. Some of the lesions on the face are not erythematous but gray, and they show an indication of a central depression. Scattered over the trunk there are several small, slightly elevated, grayish papules; none are characteristic of the lesions of molluscum but they suggest the picture of that disease. On curettage of one of these lesions, however, no caseous plug was obtained, and microscopic examination of the tissue did not show the picture of molluscum.

Note.—A subsequent biopsy by Dr. Satenstein showed lupus vulgaris.

DISCUSSION

Dr. H. C. Saunders: These lesions do not appear to me as being those of molluscum contagiosum. I believe that the eruption is caused by a drug.

Dr. John H. Harris: I saw this patient a few weeks ago. At that time the appearance of the lesions on the face and those around the forehead was somewhat different from what it is tonight. Also, on the back and arm there were definitely typical lesions of molluscum contagiosum. Numerous lesions on the forehead and on the sides of the jaw showed the effects of having been scratched. I agree with the diagnosis.

Dr. Marion B. Sulzberger: I too saw this patient a couple of weeks ago. I agree with Dr. Harris that there were lesions suggestive of treated molluscum contagiosum, but I saw no lesions of typical molluscum contagiosum. I thought that the condition was a postexanthematous disseminated lupus and left open the diagnosis of lupus vulgaris or disseminated lupus miliaris faciei. The possibility of a postexanthematous lupus vulgaris seemed to me problematic because practically all the lesions were on the face. In the cases of lupus vulgaris following the exanthems which I have seen the lesions appear preponderantly on the body. The lesions of lupus miliaris faciei are often preponderant on the face. I think that

the biopsy and the tuberculin test are the only things that will decide the question of the differentiation between lupus vulgaris disseminatus and lupus miliaris faciei. On pressure with the diascope typical yellowish nodules appeared. I suggest the two diagnoses I have mentioned.

DR. PAUL GROSS: I agree with all that Dr. Sulzberger has said. Although there was no mention of measles in the history, the mother told me that the child had measles about six months before the onset of the cutaneous eruption. I believe that the eruption is a postexanthematous lupus vulgaris.

DR. DAVID L. SATENSTEIN: It is easy to make a diagnosis of molluscum contagiosum. All that one needs to do is to scrape off a lesion, put on a drop of glycerin and look at the material. A diagnosis can be established in about a minute. A biopsy is not at all necessary.

DR. FRED WISE: Dr. Morse did make such an examination, and the results were negative. My impression when I saw this patient two or three weeks ago was that the appearance of the lesions on the face was more or less artificial. The eruption did not show the dissemination one sees in lupus disseminatus faciei or in any form of disseminated lupus. I still adhere to the idea that the patient scratched lesions of molluscum contagiosum and altered them in such a way that they appear as they do today. I believe that the mother is not aware of the scratching; perhaps the child scratches the lesions during the night. My opinion is that in all probability if a biopsy specimen were taken from the lesions on the face there would be no evidence of a lesion of molluscum contagiosum but rather the remnants of a changed lesion of that disease such as scratching would produce.

DR. JOSEPH L. MORSE: I hesitated to present this patient with a diagnosis of molluscum contagiosum because I never believed that the condition was molluscum contagiosum. This patient is difficult to manage. It took a week before I was able to examine her body. I could not make a diagnosis from the lesions of the face. My first tentative diagnosis was that of an eruption due to iodide. There was a history that iodized salt had been used. But I could not even definitely make a diagnosis of an eruption due to iodide. When the lesions on the body were examined, Dr. Wise and Dr. Harris thought that the disease might be molluscum contagiosum. Dr. Sulzberger saw the patient and made a tentative diagnosis of lupus vulgaris of the postexanthematic type. The child had measles before the onset of the eruption. There was some yellowish discoloration on pressure with the diascope, but I could not see any typical apple jelly nodules. I therefore hesitated to say that the disorder was lupus, but tonight I am more inclined to make that diagnosis. Today I managed to scrape off one of the lesions on the back with a curet. This child is extremely difficult to handle; she cries and refuses to undress. When the lesion was curetted it certainly did not show the characteristics of a molluscum lesion. A caseous plug did not pop out as happens when lesions of molluscum are curetted. I looked at the tissue under the microscope, and I did not see anything that looked like the picture of molluscum contagiosum. I do not know how I can possibly obtain material for a biopsy from this difficult child, but that is the only way in which a diagnosis can be established in this case. The patient is perfectly well. She has been under the care of a pediatrician ever since her birth, and there has been nothing wrong with her at any time. I shall try to make a tuberculin test and a roentgen examination of the chest.

LEPROSY. Presented by DR. ANTHONY CIPOLLARO.

G. A., a man aged 48, born in Turkey, of Greek parentage, has been in the United States for the past twenty-five years. He was presented at the meeting of the Atlantic Dermatological Conference on Nov. 17, 1934, by Dr. George M. MacKee.

The patient was first seen at the clinic for cutaneous diseases of the New York Post-Graduate Medical School and Hospital on Oct. 21, 1931, at which time he

presented a generalized eruption of three years' duration. He did not return to the clinic until Jan. 30, 1933. He again discontinued his visits and returned on Oct. 26, 1934.

At the present time the patient presents a generalized eruption involving the face, trunk and extremities. The eruption consists of plaques which are brownish red, slightly elevated, smooth and not scaly. On the forehead, between the eyebrows, is a pea-sized, soft, smooth, pinkish nodule. This nodule has developed within the past six months. On the anterior surface of both legs are many pinhead-sized, rather dark brown, subcutaneous nodules which have been present for several years. The plaques on the face so exaggerate the normal markings as to give the patient a leonine facies.

There is marked diminution of sensation to pinprick and temperature and of tactile sensation on the anterior and posterior aspects of both legs, on the anterior surfaces of both thighs and in the lobes of the ears. There are no other abnormalities.

Between May 1, 1934, and June 14, 1934, the patient received six roentgen treatments, each of one one-quarter skin unit, to the back. This treatment produced slight, if any, involution of the lesions.

The blood count showed 4,720,000 red blood cells, 107 per cent hemoglobin, and 6,550 white blood cells, with 58 per cent polymorphonuclear leukocytes, 25 per cent small lymphocytes, 10 per cent large lymphocytes and 7 per cent monocytes. The Wassermann reaction was negative. On Jan. 30, 1933, a biopsy on tissue taken from the back showed histologic changes suggestive of mycosis fungoides. On Feb. 17, 1933, a biopsy on tissue taken from another portion of the back showed a picture suggestive of leprosy. On Oct. 29, 1934, material for biopsy was taken from the forehead and from the leg. The report stated that this histologic picture was suggestive of leprosy, and the causative organism was found in the tissue and in smears from nasal material.

DISCUSSION

DR. SIGMUND POLLITZER: I wish to call attention to the unusual fact that this man, who was born in Turkey, where leprosy is endemic to some extent, has been in the United States for twenty-five years. That certainly is an unusual feature in a case of leprosy. It seems likely that he acquired his disease in his native country. A period of incubation of twenty or twenty-five years is rare but not unheard of. I recall the case of an Englishman who returned from India, lived in England and showed symptoms of leprosy twenty-five years after having left India.

DR. ANTHONY CIPOLLARO: Dr. Pollitzer has brought out the interesting feature of this case, namely the fact that this man was born in Turkey, of Greek parentage, and has been in the United States for the past twenty-five years. He has never left the United States since he first came here. His eruption began about seven years ago. It is only within the past six or eight months that nodules began to develop on the face, ears and forehead. Another interesting fact is that with the marked cutaneous involvement there is no enlargement of the ulnar nerves. There is diminution of sensation to pain and temperature and of tactile sensation on the lower and upper extremities and in all the areas showing nodules, including the lobes of the ears. Hansen's bacillus was found in nasal smears and also in the tissues. The histologic picture is typical of leprosy. This patient presents the macular, nodular and anesthetic type of leprosy.

DR. HOWARD FOX: The length of the period of incubation is not proved by the fact that this man has been in the United States for the past twenty-five years. It is necessary to show that during this time he lived in parts of the United States where leprosy is not endemic. If he had been in the Gulf States for any length of time the assumption that the period of incubation lasted twenty-five years would not be proved.

TINEA VERSICOLOR (WHITE). Presented by DR. GEORGE M. LEWIS.

S. R., a blond woman aged 20, is presented from the clinic for cutaneous diseases of the New York Post-Graduate Medical School and Hospital because of an eruption on the trunk and arms of two years' duration. Brown areas were first noticed on the abdomen, two years ago. Then the eruption spread over the trunk and remained brown until after the patient acquired a sunburn a few months ago; then white areas appeared.

There are patchy areas of depigmentation on the chest and upper part of the arms, corresponding in color to that of the face and neck. The apparently normal skin of the face is much paler than the normal skin of the forearms. On the back is a palm-sized area of apparent hyperpigmentation but of a shade almost identical with that of the forearms. The areas of depigmentation on the lower and upper parts of the arms yielded Microsporon furfur. The organism was not obtained from the areas of darker skin on the arms. The center and border of the area on the back also yielded the microsporon, but the skin of the face did not.

DISCUSSION

DR. MARION B. SULZBERGER: I saw this patient for the first time this afternoon when Dr. Lewis asked me whether I thought it was worth while to present her. I said I thought the case was worth while for the following reasons: For my own personal interest I should like to find out something about what is known and what the opinions are concerning the variations in pigmentation of the skin exhibited by this patient. There is certainly not a question of diagnosis. The presence of the fungi has been demonstrated. The patient has a fungous infection caused by M. furfur, a fungus which cannot be cultured with methods available at present. By looking at this patient closely it can be seen that the skin of the arms is rather brown and that, disseminated in the brownish areas, there are oval and round areas of lighter-colored skin. The question is whether the lighter skin is depigmented or not. When the areas of lighter skin are compared with the darker skin in adjacent areas it becomes evident that the areas are less pigmented than the surrounding ones. However, when they are compared with the skin of the patient's face or back, it appears that the lighter areas are the normal color of the skin. The answer seems to be that the fungous sheath has protected the skin in the lighter areas and prevented pigmentation from sunburn. However, on looking at the back, it is seen that the entire back with the exception of one area is also light. Thus one has to assume that the fungous sheath covered the face and the whole back except one small area on the back. In other words, on this assumption it is taken for granted that the fungous sheath extends over the arms, face and back except for one small area. This is not the case.

I believe, and Gougerot and others have stated, that M. furfur destroys the cutaneous pigment. I think that this theory is substantiated by the fact that while in some cases pigmentation can be restored rapidly by medication with oil of bergamot plus ultraviolet irradiation and other measures, in some cases infection with M. furfur acts like vitiligo in that pigmentation cannot be restored. I have asked Dr. Laidlaw to make some tests for dopa reactions on such patients. The results were not conclusive, but such tests have been done by others, and they demonstrate that the pigment-forming oxidase has been affected (*Year Book of Dermatology and Syphilology*, Chicago, Year Book Publishers, Inc., 1932, p. 29; 1933, pp. 26 to 28). I think that it would be worth while to check that work and continue it. This fungus may prove to destroy pigment without scarring and may some day be useful clinically.

DR. A. BENSON CANNON: This type of leukoderma is seen frequently, and the history is almost invariably that the depigmentation followed exfoliation of the skin from sunburn. I am inclined to think that the most likely cause of these light-colored spots is the use of cosmetics plus exposure to the rays of the sun. I saw a woman a few days ago with exactly the same type of depigmentation; she stated that the white spots had appeared after she had applied a lotion to

prevent tanning and exposed her skin to the rays of the sun. The patient presented may have tinea versicolor, but I cannot possibly see that that condition has any connection with the leukoderma.

DR. PAUL BECHET: I may be able to answer partially some of the questions of Dr. Sulzberger because recently there came under my observation a case similar to this one. On section no M. furfur was found in the depigmented areas. The organism was found in scrapings from the depigmented areas and was not found in material from the hyperpigmented areas. Apparently these cases appear more frequently than formerly, probably because of the sun-bathing which is practiced more and more often every summer. I think that the depigmentation is probably due to shielding by the microsporons. The areas thus affected appear depigmented, and those not covered by the organisms remain hyperpigmented. Another point I wish to bring up is one concerning the name given to this condition. I do not think that the name parasitic achromia is appropriate at all. Costello and his co-workers used the term to describe the whitish patches which occur on the faces of a great many Negro children. The fungus found was Aspergillus, and not M. furfur. Dr. Fox also reported a number of similar cases from the Harlem Hospital and has seen many cases like those described by Costello.

DR. HOWARD FOX: This case which has been microscopically proved to be one of pityriasis versicolor does not in my opinion suggest in any way the condition described by Pardo Castello as parasitic achromia. The latter disease affects chiefly the face and is common in Negro children in New York as well as in many tropical countries. In the majority of cases, of course, no fungus of any kind can be found.

DR. DAVID L. SATENSTEIN: In answer to Dr. Cannon, I must say that this patient must be clever to be able to acquire the tan in the definite spots to produce this type of lesions. I am rather surprised to hear a discussion along this line. All the members know of freckles. If the sun's rays can cause increased pigmentation, I cannot see why they cannot do the opposite. When hyperpigmentation due to sunburn disappears, the area is usually mottled, not uniform. The skin appears dirty. This condition is similar to that which is known as freckles, a disorder in which there is an increase in pigmentation. It is not unusual to find the microsporons in patients with dark skins, who do not know they have them. I think that Dr. Sulzberger's theory that the microsporons produce a shield which protects the skin from the rays of the sun is rather fanciful. The sun's rays affect the entire thickness of the epidermis down to the deeper zones, and if their action can penetrate through the horny layer, it can also pass through this layer of organisms in the horny layer. That is where the organisms are usually found. The theory is far-fetched.

DR. CHARLES WOLF: The hypotheses Dr. Sulzberger brought out are interesting. The ultraviolet portion of the sun's rays is easily filtered out by any type of interference, and it is possible that the parasites lodged in the skin may be able to eliminate that part of the rays. That fact may account for the lack of pigmentation occurring where the parasites are. My opinion was that M. furfur inhabited the superficial portions of the skin and was not inclined to circulate in the blood stream. As the result of this superficial covering with microsporons the layer of melanoblastic cells may become dormant because of the lack of direct stimulation.

DR. DAVID L. SATENSTEIN: How about the pigmentation in the parts of the bodies of Negroes protected by clothing? How about the pigmented areas around the nipples. I do not quite understand the theory.

DR. HENRY D. NILES: I am much in favor of the toxic theory to explain the depigmentation, for the following reasons: There are reports of several cases of pityriasis versicolor with depigmentation in areas which were covered and had no chance of being affected by filtered rays of the sun. Another point is that pigmentation is not restored in these depigmented areas when they are exposed to ultraviolet radiation. Another theory that is plausible is that there is at first an overactivity of pigmentation which is followed by temporary paralysis or lack of pigmen-

tary power. I think that the toxic process may be considered similar to that which occurs in syphilis and psoriasis, that is, in leukoderma syphiliticum and psoriaticum.

DR. A. BENSON CANNON: Every year I see two or three dozen cases of leukoderma similar to that of the patient presented tonight, and I am impressed with the fact that the condition is almost invariably seen in women, and especially in those who are well to do and are accustomed to using many cosmetics. In each instance the leukoderma has followed exfoliation of the skin from sunburn. The pigment has always returned, and often restoration of the pigment has followed the application of oil of bergamot to the depigmented areas plus exposure to the rays of the sun or to ultraviolet rays from the air-cooled quartz mercury vapor arc. I have never noticed the presence of tinea versicolor in any of these cases.

DR. MARION B. SULZBERGER: I shall not argue with Dr. Satenstein about the theory of filtration and protection from the light. If it is fanciful, it is not a product of my fancy. It has been a long accepted theory. The other point is this. There have been, as Dr. Niles has said, cases of this kind in Negroes who have used no cosmetics of any kind but who have had this fungous disease, and in such patients the areas affected became lighter than the normal Negro skin. Therefore there must be something in this fungus that actually removes pigment from the skin. Hence I agree with those who state that the simple screening action of the fungus covering is not the entire or adequate explanation for the origin of the lighter areas.

DR. GEORGE M. LEWIS: The reasons in favor of a toxic origin for the lighter areas have been detailed by Dr. Sulzberger and Dr. Niles. However, if fungi are still present in apparently cured areas, this alone may account for the continued lack of color. The interesting features in this patient include the varied mycologic findings and the similarity in shade between the "depigmented" areas on the arms and chest and those of "normal" skin on the face. A distinction may be drawn between the light color in these areas and the absence of color in true vitiligo.

SECONDARY SYPHILIS (SHOWING THE RESULT OF TREATMENT WITH POTASSIUM IODIDE). Presented by DR. H. C. SAUNDERS.

H. S., a man aged 31, was previously presented from the University and Bellevue Medical College Clinic at the meeting of this section on November 7 (this issue, page 891).

This patient has been treated with potassium iodide. At the beginning of treatment he took 5 drops of a saturated solution of potassium iodide three times a day; now he is taking 20 drops. At present the lesions have almost completely disappeared.

DISCUSSION

DR. SIGMUND POLLITZER: I am pleased to see this patient this evening. It does not often happen that patients who have been presented are seen again. I am particularly glad to see this patient because when he was presented four weeks ago I insisted that his lesions were due to syphilis. The results of the therapy bear out that diagnosis. The large infiltrated lesions have almost disappeared. It is interesting to note that this result was brought about by the use of potassium iodide. The patient had extensive good antisyphilitic treatment before without results. I think it is worth while to bear in mind that this old remedy, which was formerly in such high repute and is nowadays employed rather seldom, was of such value in this case.

DR. CHARLES WOLF: As the members will recall, last month this case created quite a discussion. I was one of those who thought that the lesions might be tuberculids. Although there has been great improvement, one cannot absolutely say that the disorder was a manifestation of a stage of secondary syphilis. It is known that medication with iodides improves tuberculids; for instance, Bazin's disease, including ulcerative lesions, can be cleared up by rest in bed and administration of iodides. The improvement does not absolutely prove that this is a case of syphilis until this eruption has entirely disappeared. I think that the case requires further observation and that the patient should be presented again. All the members should be grateful to Dr. Saunders for presenting this patient again.

DR. LOUIS CHARGIN: In my discussion of the case last month I expressed the opinion that the eruption was some type of syphilis, although I was unable to definitely identify it. Tonight it may be definitely stated that the disease is corymbiform syphilis, as it shows the usual large papule with surrounding follicular lesions.

DR. PAUL GROSS: If I remember correctly I said that this case was one of corymbiform syphilis. If the condition were tuberculous, it could be only lupus vulgaris, which would not respond so promptly, if at all, to medication with potassium iodide.

DR. HOWARD FOX: This patient is from the clinic at the Bellevue Hospital; he was presented recently at the meeting of the Atlantic Dermatological Conference. There was some difficulty as to the diagnosis because in infancy the patient had had a tuberculous condition of the ankle, although there is no active tuberculosis now. He came to the Bellevue Hospital with a maculopapular syphilid and was treated with neoarsphenamine, a bismuth preparation and mercury. Administration of neoarsphenamine had to be discontinued because of severe nitritoid reactions. The original eruption cleared up, and then this lenticular papular eruption appeared while the patient was still under treatment. He was given further treatment with mercury and a bismuth preparation, which did not seem to have much effect. There was no improvement until he began to receive potassium iodide. The man is far from well, though he undoubtedly shows improvement. Dr. Riordan submitted the histologic section to Prof. Alexander Fraser, who considered the changes in the blood vessels characteristic of syphilis.

DR. H. C. SAUNDERS: I present this patient again tonight to show that his lesions did improve under antisyphilitic treatment and that the diagnosis of syphilis has been substantiated. In addition, I wish to show the results obtained with administration of iodides. It is interesting to note that this patient had received sixteen injections of neoarsphenamine and that this eruption appeared between the sixth and the seventh treatment. His disorder did not respond to neoarsphenamine, a bismuth preparation or mercury, but it did respond to iodides. It is also interesting to note that the general condition of the patient is much improved.

PRIMARY SYPHILIS. RECURRENCE? REINFECTION? Presented by DR. LEO SPIEGEL.

A chauffeur, aged 25, first came to the dispensary of the Lenox Hill Hospital on April 26, 1934. He complained of a sore on the penis which had been present for about one week. He stated that he had had sexual intercourse about two weeks previously.

Examination showed three superficial erosions of the size of a split pea, two being located on the glans and the third, on the shaft of the penis, about 2 cm. from the corona. A provisional diagnosis of herpes was made. The Wassermann reaction of the blood was negative with both alcoholic and cholesterolized antigens. The Kline reaction was plus-minus with the diagnostic antigen and 3 plus with the exclusion antigen. No dark-field examination was made as the patient was late in arriving at the clinic. A physiologic solution of sodium chloride was applied, and the patient was instructed to return at the following session of the clinic. He presented himself one week later, on May 3. Dark-field examination gave negative results with material from the lesions on the glans, but the lesion on the shaft of the penis showed numerous spirochetes (Spirochaeta pallida). There were no palpable glands. The Wassermann reaction of the blood was again negative with two antigens, and the Kline test gave a negative and a plus-minus reaction with diagnostic and exclusion antigens, respectively. Intensive treatment was immediately instituted. From May 3 on the patient received twelve injections of silver arsphenamine, the first four within five days, one of 0.1 Gm. and the subsequent ones of 0.2 Gm. each. A soluble preparation of bismuth in oil was also given during the course of the arsenical therapy, the patient receiving in all seventeen injections of 1 cc. each from May 3 to July 20. The Wassermann and the Kline reactions of the blood were both negative with their respective two

antigens on June 20. From July 27 on the patient received a course of twelve intravenous injections of arsphenamine of 0.2 Gm. each, the last injection being given on October 22. The Wassermann and Kline reactions of the blood were again negative on October 29. On November 19 the second injection in a second course of bismuth therapy was administered.

The patient asked to be examined on November 27 and stated that about four days before he had noticed an eruption on the body. The penile sore had appeared ten days before. He admitted having had several sexual exposures during the latter part of October 1934. When confronted with the fact that she had been the cause of his illness, the partner admitted that she had been receiving "shots" at a city clinic.

Examination showed a profuse macular syphiloderm and an inguinal satellite adenopathy on the right side. Dark-field examination of the penile lesion again showed spirochetes. The new lesion was situated midway on the under-surface of the shaft of the penis. It was the size of a pearl button and hard and infiltrated. The Wassermann reaction of the blood was negative with two antigens. The Kline test gave a plus-minus reaction with the diagnostic and a 1 plus reaction with the exclusion antigen. Three subsequent Wassermann tests were negative with two antigens; the Kline test performed with the same specimens of blood gave the following reactions: 1 plus, 3 plus and 2 plus with the diagnostic antigen and 2 plus, 3 plus and 4 plus with the exclusion antigen. On December 1, the Kahn reaction was plus-minus.

DISCUSSION

Dr. A. Benson Cannon: I should regard the case as one of recurrent secondary syphilis in an inadequately treated patient. I think that the lesion on the penis as well as the eruption on the body are manifestations of secondary syphilis. I believe that Hoffman, Stokes and others have enumerated a number of definite requirements necessary for reinfection—rules that are too well known to need to be stated. I believe that this case in no way meets these requirements, and hence the diagnosis of reinfection should not be considered.

Dr. H. C. Saunders: I think that for this case to be classed as one of reinfection a negative reaction of the spinal fluid should have been obtained. I agree with Dr. Cannon.

Dr. George M. Lewis: For the reasons advanced by previous speakers, the evidence appears to indicate a diagnosis of relapse manifested by cutaneous symptoms.

Dr. Adolph Rostenberg: I also think that this case cannot be regarded as one of reinfection, owing to the short interval between the appearance of the two lesions. I think that there should have been a much longer interval between the manifestations if they were to be regarded as caused by two infections.

Dr. Louis Chargin: I agree with the remarks of Dr. Cannon. All the conditions necessary for establishing the case as one of reinfection are apparently lacking.

Dr. Eugene J. Bernstein: I think that this patient has a typical reinfection. I cannot believe that the lesion on the penis is secondary; it is typical of a primary lesion and appeared after the typical interval of time following exposure, like a new infection. Three weeks after the second exposure this primary lesion appeared, and then a generalized eruption developed. I do not think it is fair to say that this is a recurrence because of the fact that spirochetes were found in the first primary lesion. After the second exposure three weeks elapsed before the appearance of this primary lesion which was followed by a generalized eruption.

Dr. Leo Spiegel: I admit that it is rather difficult to prove that this case is one of reinfection, but if one accepts the evidence of the repeated negative Wassermann reactions throughout the period of the first infection, disregarding the Kline precipitation test which gave a 3 plus reaction with the exclusion antigen and one week later a plus-minus reaction with the same exclusion antigen, the patient having up to that time received no treatment, the criteria may be complied with.

This patient was carefully followed, and the clinical data of his first infection were stated in the history. I believe that this patient achieved a biologic "cure" in his first infection, and while such cures cannot be interpreted as absolute, nevertheless I believe that according to the present knowledge and conception of this disease, the case should be reported and accepted as one of probable clinical reinfection.

The clinical criteria for proof of reinfection as outlined by Stokes and his co-workers (Stokes, J. H.; Schoch, A. G., and Ireland, F. A.: The Clinical Concept of Reinfection in Syphilis: A Critique Based on Five Cases, the Reported Literature and a Study of Early Relapse, Treatment of the First Infection, ARCH. DERMAT. & SYPH. **23**:829 [May] 1931) are considerably more stringent than those laid down by Halley and Wassermann and by Bernard (Halley, C. R. L., and Wassermann, H.: Second Infection in Syphilis: Its Relation to the Time of Infection, *Arch. Int. Med.* **41**:843 [June] 1928. Bernard, R.: Réinfection syphilitique; pseudoréinfection-superfection, *Bruxelles-méd.* **7**:72 [Nov. 7]; 105 [Nov. 21] 1926). I have made notations of the various criteria and shall apply them to this case as follows:

1. The presence of the original infection must be proved either by positive results of dark-field examination or by a definitely positive Wassermann reaction of the blood. In this case the dark-field examination gave positive results.

2. A complete physical examination must have been negative for signs of syphilis after treatment for at least two years after the onset of the first infection. The first part of this criterion is complied with; the time factor of two years, however, does not apply in this case, for, I believe, it was previously stated that the case may have been one of biologic "cure." This is probably a weak link in my efforts to prove that it is a case of reinfection.

3. The third criterion, namely, a negative Wassermann reaction of the blood for one year after the cessation of treatment does not apply in this case if one takes into consideration the concept of biologic "cure."

4. This criterion concerns the reaction of the spinal fluid. It is the weakest link in the conception of this case as one of reinfection because the cerebrospinal fluid had not been examined up to the time of the appearance of the second chancre and of the secondary eruption. While I believe that in all probability the reaction of the spinal fluid would have been normal had it been examined before the inception of the second infection, I think that I was not justified in examining the fluid while the patient showed clinical signs of secondary syphilis. While a normal reaction of the spinal fluid would possibly favor the assumption that the case was one of reinfection, a positive reaction would not indicate the time at which the cerebrospinal axis was invaded. I intend to examine the spinal fluid as soon as the patient has had more treatments.

5. No evidence of any form of relapse due to the first infection should appear in the period between the two infections. This criterion is met in the case under consideration.

6. A definite history of exposure preceding the second infection must be obtained. That point too is met.

7. A demonstration of the infectious condition of the supposed source of infection must be had by confrontation. This requisite is complied with.

8. There must be a period of incubation of from seven to forty days between the date of exposure and that of the appearance of the second primary lesion or lesions. That point is met.

9. The ninth criterion was complied with, as the second primary lesion appeared on a different site from the original primary lesion.

10. The tenth criterion was also complied with, as no signs of activity developed at the site of the original primary lesion.

11 and 12. The eleventh and twelfth criteria are met, as positive results were obtained when material from the second primary lesion was subjected to dark-field examination and a satellite adenopathy developed under observation.

13. The negative Wassermann reaction of the blood must change to positive under observation while the chancre is present. That criterion was complied with in that the slide precipitation test of Kline gave positive results with both antigens although the Wassermann reaction remained negative.

14. Secondary manifestations must appear not less than twenty days after the second primary lesion. That criterion has been complied with.

15. As regards treatment, the fifteenth criterion was fulfilled in that twenty-four injections of arsphenamine and nineteen of a bismuth preparation had been given within a period of seven months.

16. The criterion which requires that the interval of time between the onset of the first and the second infection should be sufficient (at least two years) to exclude the large proportion of relapses, cannot be applied, as no positive serologic reactions were obtained and, as previously mentioned, this case represents a biologic "cure."

17. Lastly, the symptoms of both infections must have been observed by the same competent physician or by two competent physicians using modern methods. I do not know whether the last criterion can be applied or not, but I hope it can.

DR. ISADORE ROSEN: This is really an important case. I do not think that it should be recorded as one of reinfection. Dr. Spiegel gives an interesting enumeration of the factors necessary to establish a diagnosis of reinfection, but I do not think that all these requirements are met in this case. I note that Dr. Spiegel has failed to examine the spinal fluid during the period of this patient's first infection. That, in my opinion, rules this case out as one in which a cure had been established. He states that it is not important whether a patient has a positive reaction of the spinal fluid or not. I have seen a number of patients with syphilis who have had a negative reaction of the blood and a positive reaction of the spinal fluid when the disease was treated early. These cases may go on indefinitely, and clinical manifestations may develop at any time. According to this patient's history a primary lesion first developed on November 27, and six or seven days later a secondary eruption appeared. It is certainly unusual to see a secondary eruption follow the appearance of a primary lesion so rapidly.

DERMATITIS MEDICAMENTOSA (CHLORAL HYDRATE). Presented by DR. LOUIS TULIPAN.

E. B., a woman aged 65, was presented at the meeting of the Section of Dermatology and Syphilis of the New York Academy of Medicine (meeting of November 7; this issue, page 888) because of an eruption following the ingestion of a mixture of bromide and chloral.

Since the patient was presented patch tests with a 5 per cent solution of chloral hydrate and a 5 per cent solution of sodium bromide, respectively, have been made. Forty-eight hours after the application of the chloral hydrate solution, a marked eczematous reaction was seen in loco, and the patient complained of generalized tingling and some discomfort. No reaction was observed after the application of the sodium bromide solution. This proves that the diagnosis of an eruption due to chloral hydrate was correct.

URTICARIA PIGMENTOSA IN AN ADULT. Presented by DR. B. F. FELDEN.

M. S., a French woman aged 43, presented herself for the first time today at my office. Her cutaneous disorder began twenty years ago, without any apparent reason. She presents on the trunk and on all the extremities hundreds of oval or roundish, well defined, brownish or brownish red macular lesions the size of a split pea or larger, which swell up when rubbed and change from macules into papules. There is moderate dermographism. She was treated unsuccessfully in a hospital in Paris with injections of her own blood and roentgen irradiation.

BRONX DERMATOLOGICAL SOCIETY

HENRY SILVER, M.D., *Secretary*

Regular Meeting, Nov. 22, 1934

LOUIS CHARGIN, M.D., *President*

GENERALIZED TELANGIECTASIA (FORME FRUSTE OF RECKLINGHAUSEN'S DISEASE?). Presented by DR. ADOLPH ROSTENBERG.

This girl, aged 15, had hemorrhagic measles in early childhood; the present cutaneous disorder is said to have developed after that illness. The family history is irrelevant.

The patient presents on the face, arms, chest and back a large number of discrete vascular dilatations varying from the size of a pinpoint to several millimeters in diameter. They are flat and resemble "port wine stains." Besides these vascular lesions many moles and freckles are present in the same areas.

The mental development of the patient is normal. Physically she is underdeveloped and looks like a child of 10.

DISCUSSION

DR. SAMUEL M. PECK: The patchy vascular condition—it cannot be called an eruption—certainly resembles a naevus flammeus. The patient states that she suffered from frequent nasal hemorrhages. The father and sister had a similar history. I could not look into the nasal canal, but it is important to ascertain whether telangiectasia is present there. The lesions may be a hereditary telangiectasia and also a nevoid condition, rather than a forme fruste of Recklinghausen's disease.

DR. F. E. CROSS: I am under the impression that this is a nevus regardless of the previous history, because the eruption is mostly unilateral.

DR. HENRY SILVER: Clinically it is a typical case of generalized telangiectasia, but not of the type described by Osler, and I should hesitate to obscure this picture by bringing up the question of forme fruste of Recklinghausen's disease.

In the etiology of generalized telangiectasia such factors as endocrine disorders, toxemias and circulatory disturbances are mentioned. It is plausible that a severe toxic exanthem (hemorrhagic measles) can produce this type of telangiectasia.

DR. D. L. SATENSTEIN: The condition to which Dr. Peck refers is Osler's familial telangiectasia, which was described in about 1907. The appearance of this patient's lesions does not correspond to the description given in numerous reports of cases; in those cases the lesions described were associated with real angiomas. I have seen patients with many lesions on the face, tongue, lips and mucous membranes, and these have occurred in as many as from twelve to fifteen members of a family. If the history can be accepted and the eruption developed after an attack of measles, I should be more inclined to accept the possibility of a tuberculous type of eruption associated with telangiectasia. However, I do not get that impression. The condition is of the naevus flammeus type.

DR. C. LERNER: I cannot agree with the diagnosis as presented, and I am inclined to regard the process as the manifestation of an endocrine disturbance. The bleeding from the nasal mucosa may be considered vicarious menstruation. Whether the attack of measles played any part in the production of the telangiectatic lesions is, of course, conjectural.

DR. ADOLPH ROSTENBERG: I should like to stress that this is not a unilateral nevus. The lesions are widely spread all over the body. I can definitely state that no other members of the family are similarly affected, nor is there a history of nosebleed in the patient or in the family. Therefore, I do not think that the condition fits into the group of Osler's type of telangiectasia. The reason I mention the forme fruste of Recklinghausen's disease is because of the presence of the many freckles and moles.

DARIER'S DISEASE IN FOUR MEMBERS OF ONE FAMILY. PRESENTED BY DR. HENRY SILVER.

Miss J. V., aged 20, was admitted to the clinic for cutaneous diseases of the Mount Sinai Hospital on Aug. 18, 1934. She first noticed some brown "spots" on the left side of the neck about three years ago. No other lesions were seen until about two months before admission, when in a short time many rough, brown lesions appeared on both sides of the neck, face and trunk. There were no subjective symptoms.

An inquiry into the family history revealed that the patient's mother and her two sisters were suffering from the same disease. The older sister, a young married woman, refused to submit to an examination.

The patient presents a widespread eruption. It is localized on the lateral aspects of the neck and over the temples, whence it extends for a short distance back into the scalp, in the axillae, in the intermammary and in the genitocrural regions. It consists of papules from the size of a pinpoint to that of a pinhead which are follicular, hyperkeratotic, dark brown to grayish and slightly scaly and have definite nutmeg-grater feel. There is a marked seborrhea of the scalp.

The mother, an Italian woman aged 52, presents a somewhat milder eruption. The lesions on the temporal and intermammary regions are firmer to the touch and are more typical of the disease.

The one sister, aged 18, presents a few areas with the characteristic follicular, hyperkeratotic lesions.

The study of sections from lesions of the patient and the mother corroborated the clinical diagnosis of Darier's disease.

MYCOSIS FUNGOIDES. Presented by DR. ADOLPH ROSTENBERG JR.

R. S., a housewife, aged 52, states that her eruption appeared in 1922 and gradually became generalized.

From 1922 to 1928 she was a patient of many clinics for cutaneous diseases in this city. She was admitted to the Montefiore Hospital on Dec. 3, 1933. In the beginning the eruption consisted of dry, slightly raised, somewhat itchy, scale-free areas of various sizes. Exposure to sunlight, autohemotherapy and administration of arsenic improved the condition somewhat, but flare-ups occurred regularly. During the past three years the itching became severe.

The clinical diagnosis on admission was generalized eczematous stage of mycosis fungoides. A biopsy made at that time suggested the inflammatory stage of mycosis fungoides. Since March 1932 the clinical aspect of the lesions had changed. Scattered over the body were many tumor-like lesions from the size of a pea to that of an almond. Also some of the erythrodermic areas appeared to be more infiltrated. The clinical diagnosis of mycosis fungoides became more probable. Another biopsy, made on April 17, 1934, definitely established the diagnosis of the tumor stage of mycosis fungoides.

Fractional roentgen treatment was instituted and a total of two erythema doses (600 roentgens) given to each area. After this treatment the number of white blood cells decreased from 8,200 to 2,300. At present there are 3,900 white cells.

DISCUSSION

DR. D. BLOOM: The diagnosis can be decided only by histologic examination. Unless the histologic picture distinctly indicates mycosis fungoides, I should consider the eruption clinically as psoriasis. A number of lesions show the typical picture of psoriasis. The fact that many lesions do not show scaling may be explained as a result of previous application of ointments.

DR. L. SPIEGEL: My first impression was that the condition is mycosis fungoides. The reason is as follows: There are a number of plaques which, although infiltrated, are unevenly so. This is characteristic of mycosis fungoides. The histologic picture bears out the clinical impression.

DR. F. E. CROSS: I believe that the condition is Duhring's disease. The long duration, the urticarial background, the grouping and the severe itching point to that diagnosis. According to the patient's statement, the lesions start as vesicles. I certainly do not believe that the picture is that of mycosis fungoides.

DR. D. L. SATENSTEIN: The question of prefungoid mycosis fungoides has been a subject of dispute for many years. If there is a special pathologic picture in the prefungoid stage it is not recognized at the present time. Mycosis fungoides has a fairly definite pathologic picture. Unless this is found, the disease cannot be called mycosis fungoides. I recall having observed cases at the Vanderbilt Clinic, where for years numerous biopsies have been made. Mycosis was never found, but eventually definite mycosis fungoides was demonstrated. As far as this patient is concerned, I cannot see any signs suggestive of Duhring's disease. There are no grouped papular lesions, and no pigmentation is present.

DR. SAMUEL FELDMAN: There is no particular disease or particular condition in which the action of the roentgen rays on the white blood cells is different from the action in any other disease. That means that if roentgen rays cause leukopenia they can cause leukopenia in any condition that is treated roentgenologically. If massive doses of roentgen rays are given and the treatment is continued for a long time, leukopenia will develop in mycosis fungoides as well as in any other disease.

DR. M. UMANSKY: After massive doses of roentgen rays are applied, various changes in the composition of the blood can be observed. Besides leukopenia a reduction in the hemoglobin content and a decrease in the number of red cells can be found.

DR. C. LERNER: Since the effects of irradiation on mycosis fungoides have been mentioned, I should like to stress two points: first, that roentgen rays have a tendency to drive the leukocytes from the peripheral circulation into the splanchnic area, thereby causing leukopenia; second, that any toxemia that develops in a case of mycosis fungoides is more likely to be the result of too rapid an absorption of the tumors, which throws a strain on the excretory organs of the body, than of the irradiation per se, particularly when the dosage is cautiously watched, as I understand it has been in this case. It is also important to bear in mind in this connection that as the irradiation is continued its effectiveness gradually diminishes until it becomes almost worthless.

DR. LOUIS CHARGIN: I have been interested in the problem which Dr. Satenstein mentions. Some time ago I studied the literature of the past several years in order to ascertain whether I could discover a case in which the condition was labeled prefungoid mycosis fungoides clinically and eventually terminated in mycosis fungoides. I found a report of one such case by Arzt. The pathologic picture in the case was not specific at first but became so as time progressed. I feel certain that there are many such cases.

DR. D. L. SATENSTEIN: Quite a few cases of radiosensitivity have been observed. Patients become ill, and some vomit after irradiation of large areas; probably this reaction is due to a rapid breaking down and absorption of protoplasm. In 1920 or 1921 it was stated that the roentgen rays caused a decrease in the number of leukocytes of the blood. It was shown and proved that the number may decrease to 3,000 or 4,000 in forty-eight hours and then return to 6,000, 7,000 or 8,000. If the change occurs after a single exposure it may also occur after repeated exposures. Whether it is transitory or permanent, I do not know.

DR. THEODORE ROSENTHAL: The clinical appearance of the lesions, the bizarre arrangement and the history that the disorder lasted from twelve to thirteen years are, I think, sufficient evidence to justify a diagnosis of mycosis fungoides.

DR. ADOLPH ROSTENBERG JR.: As far as the comments on leukopenia are concerned, most of the points were recently discussed. I am inclined to agree with Dr. Feldman that whether or not it develops depends on the size of the roentgen dose more than on the type of lesion that is being treated. This patient never received a massive dose, and the treatments were spread out over quite a period of

time. As far as toxic absorption from broken-down tissue is concerned, that can cause systemic effects, but whether or not it would cause leukopenia is doubtful.

A Case for Diagnosis (Unilateral Nevus or Lichen Planus). Presented by Dr. Eugene F. Kelley.

J. W., a man aged 21, presents an eruption on the right buttock which has existed since he was about 4 months old. Subsequently lesions appeared in the right axilla and on the right side of the chest. There has been no change in the lesions during the past eighteen months.

A bandlike lesion from ½ to ¾ inch (1.2 to 2 cm.) wide extends from the right buttock along the back of the thigh. On the right buttock there are coin-sized lesions. These patches consist of pinhead-sized violaceous papules which have coalesced. In the axilla these papules have formed patches from the size of a split pea to that of a pea, and on the right side of the chest all the lesions are discrete and acuminate, varying from the size of a pinpoint to that of a pinhead, and the eruption ends abruptly at the midline of the chest.

Histologic examination by Dr. Machachek of a lesion excised from the right buttock showed definite hyperkeratosis and parakeratosis. The granular layer was absent beneath the parakeratotic portions. The follicular funnels were dilated and filled with keratin. The rete cones were elongated. The rete was edematous. The corium contained a few chromatophores, although the melanin was not always distinguishable in the basal layer. The superficial corium was edematous and infiltrated by round mononuclear cells, some of which were plasma cells. The histologic diagnosis was epidermal nevus.

DISCUSSION

Dr. C. Wolf: I wish to state that the lesions on the side of the chest do not appear to be nevi in the true sense of the term. They are discrete, spinulous and inflammatory.

Dr. C. Lerner: I could not see any lesions that had any definite nevoid character. When the patient was questioned he stated that he had a small lesion on the buttock ever since he was 3 or 4 years old. However, the major part of the linear patch extends downward on the back of the leg and has been present only for the past two years. This condition may well be a linear lichen planus. The lesions under the right axilla appear more like lichen spinulosus.

Dr. M. Umansky: The eruption on the buttock and leg resembles a linear neurodermatitis. The lesions in the axilla are of a somewhat different character but could fit in with the diagnosis of Fox-Fordyce's disease, which, according to some authors, is a type of neurodermatitis.

Dr. F. E. Cross: In view of the marked keloid which appeared after excision of the biopsy specimen and because of the location of the nevus I think that treatment should be withheld.

Dr. Eugene F. Kelley: The lesions on the buttock appeared when the patient was 4 months old. Those on the chest resemble the lesions on the buttock in color only and terminate abruptly at the midline. The lesions in the axilla have a nodular aspect and resemble those of lichen planus. They appeared along with the lesions on the chest four years ago. There has been no change in the two years in which I have observed the patient.

Keratoderma Palmare et Plantare. Presented by Dr. Adolph Rostenberg Jr.

This woman, aged 64, states that the cutaneous disorder has been present as long as she can remember and that her father suffered from a similar malady.

There is a diffuse thickening of the skin on both palms, extending to the fingertips and terminating sharply at the wrists. This process seems to involve the horny layer symmetrically on both hands and both feet. The dorsal surfaces appear somewhat wrinkled and indurated. All the nails are also involved; they

appear thickened and are markedly hyperkeratotic. There is marked hyperhidrosis. The soles are similarly affected but show, in addition, patches covered with thick grayish adherent scales which cause pain on manipulation.

There seems to be considerable hyperpigmentation over the entire body.

The patient has never taken any drugs containing arsenic. No arsenic was found in the urine.

DISCUSSION

DR. C. WOLF: I think that the patient has enough signs at the present time to indicate that there may be an arsenical background. Hyperpigmentation on the sides of the neck and keratoderma of the hands and feet are present. Arsenical keratosis must be considered.

DR. ADOLPH ROSTENBERG: The patient has never taken arsenic, and the chemical analysis of the urine for the drug gave negative results.

A CASE FOR DIAGNOSIS (TERTIARY SYPHILIS OR PSORIASIS?). Presented by DR F. E. CROSS.

S. W., a peddler aged 52, states that he had a chancre on the shaft of the penis thirty-five years ago. He has received no treatment up to the present time. He was operated on at the Mount Sinai Hospital for hypertrophy of the prostate in February 1931. The Wassermann reaction of the blood at that time was 3 plus.

Near the corona of the glans penis the patient has one sharply defined erythematous scaly patch about 1 cm. in diameter with a raised papular border. Just to the right side of the corona is a similar darker, scaly lesion about 0.5 cm. in diameter, of two weeks' duration. A Wassermann test of the blood made on Nov. 19, 1934, was reported to be 4 plus. There is no other clinical evidence of psoriasis or syphilis.

DISCUSSION

DR. V. A. CORNELL: I thought of psoriasis when I first looked at the lesion and, of course, of lichen planus, but the patient states that he has taken drugs containing phenolphthalein for some time, and that fact, together with the duration (two weeks), the location and the color of the eruption, make me think that the lesions may possibly be caused by phenolphthalein.

DR. L. SPIEGEL: This patient presents three papules—one on the glans and two similar ones back of the glans. While I do not wish to made a definite diagnosis, I do not think that the condition is syphilis. The diagnosis of psoriasis should be considered.

DR. D. BLOOM: If the short duration could be disregarded I should consider the diagnosis of erythroplasia.

DR. D. L. SATENSTEIN: I have always heard that lesions of syphilis retain their identity. This patient's lesion seems to be a fairly superficial erythematous plaque; that in itself is not a manifestation of syphilis. I am more inclined to favor a diagnosis of psoriasis. The condition may be erythroplasia.

DR. THEODORE ROSENTHAL: I think syphilis can fairly well be excluded. There is no sign of any elevation; the lesion is entirely flat, and there is no infiltration whatever. Erythroplasia can be excluded because there is no elevated velvety appearance. Most likely the disorder is psoriasis.

DR. ADOLPH ROSTENBERG: It is psoriasis. I have seen quite a number of similar cases. Syphilis can be ruled out. The lesion is not raised enough and appears too dry to be erythroplasia.

DR. F. E. CROSS: I think that the possibility of an eruption due to phenolphthalein can be definitely ruled out. It is true that the elevated border is not distinct this evening, but the patient has already taken potassium iodide by mouth and has received an intramuscular injection of a bismuth preparation. The elevated border around the lesion made me think of syphilis. One must not forgot that syphilis can reproduce the symptoms of any cutaneous disease. The diagnosis can be settled by biopsy and therapeutic test.

LUPUS ERYTHEMATOSUS (BULLOUS TYPE). Presented by DR. HENRY SILVER.

This woman, aged 36, was admitted to the clinic for cutaneous diseases of the Mount Sinai Hospital on April 29, 1933. She first noticed a scaly lesion on the scalp one year before admission. Eight months later lesions developed on the upper eyelids, on the anterior region of the chest and behind the right ear.

A diagnosis of lupus erythematosus was made, and treatment with gold sodium thiosulphate was instituted. By the end of June 1933 the eruption cleared up completely.

In July 1934 there was a recurrence. There were again typical lesions of lupus erythematosus in the areas which had formerly been involved and on the back of the scalp. In addition, there were on the chest erythematous, bullous and crusted lesions more like those of erythema multiforme than like those of lupus erythematosus. The upper portion of the arms showed semicircular, thickly crusted areas which manifested a tendency to creep upward. The lesions on the arms healed rapidly and showed no atrophy; only pigmentation persisted.

The routine laboratory examinations of the blood and urine gave negative results.

The histologic study of the section from a lesion behind the ear revealed lupus erythematosus. A section from a lesion on the upper portion of the arm showed banal inflammatory changes.

DISCUSSION

DR. D. BLOOM: The lesions on the face and scalp are typical of lupus erythematosus of the discoid type. The crusted lesions on the chest, which are due to a previous bullous eruption, suggest the bullous type of lupus erythematosus. The flat erythematous, somewhat brown pigmented patches on the arms are lesions like those seen in cases of disseminated lupus erythematosus. The diagnosis is disseminated lupus erythematosus with bullous formation.

DR. SAMUEL FELDMAN: I have seen a case of disseminated lupus erythematosus of the bullous type. The lesions on the arms, as Dr. Bloom pointed out, give one the impression of subacute disseminated lupus erythematosus.

DR. C. WOLF: An interesting feature in this case is the symmetrical arrangement of the lesions on the arms which almost cover half its circumference. It is known that lupus erythematosus can clear up and leave no signs. On the other hand, with an erythematous eruption and atrophy and scaling on the scalp, such as are present in this case, one would expect some scaling and atrophy on the arm. The fact that the lesions on the arms are so symmetrical and have cleared up spontaneously, although they appeared later than those on the face, suggests the possibility of their being factitious.

DR. C. GREENHOUSE: I agree with Dr. Bloom so far as the clinical picture is concerned. However, I should like to raise a pertinent question. Can one make a definite histologic diagnosis of acute lupus erythematosus? It is my impression that for such a diagnosis to be permissible the disease must show some degenerative changes. At this time, therefore, the case is no longer one of acute lupus erythematosus.

DR. THEODORE ROSENTHAL: Has Dr. Silver ruled out the possibility of an external dermatitis due to some irritating ointment, particularly in the case of the lesions on the chest?

DR. SAMUEL M. PECK: Lupus erythematosus of the classic type was found behind the ear. The lesions on the arm disappeared quickly after application of a bland ointment.

DR. HENRY SILVER: Dr. Wolf's contention that the lesions on the arms may be factitious because they healed rapidly without atrophy is not tenable. Rapid healing with pigmentation but no atrophy is observed in this type of lupus erythematosus. The possibility of reaction from an external irritant has been carefully eliminated. Cases of this type are recorded in the literature as instances of the Senear-Usher type of pemphigus. There is still some confusion in regard to this syndrome. It is described as a benign type of pemphigus associated with features

of lupus erythematosus. This case has many of the clinical features of the Senear-Usher syndrome. However, lupus erythematosus of the bullous type is probably the best diagnosis.

ERYTHEMA INDURATUM BAZIN (?) TREATED WITH CEVITAMIC ACID. Presented by DR. ADOLPH ROSTENBERG JR.

This woman, aged 26, born in Russia, has had her cutaneous condition for the past ten years. She suffers attacks each year with the onset of cold weather. There are periods of complete remission beginning each spring and lasting until fall.

There are multiple lesions on both legs, mostly on the lower halves and on the posterior surfaces. They consist of erythematous nodules with a bluish tinge. The lesions vary in size from that of a dime to that of a quarter.

The tuberculin test with a dilution of 1:1,000,000 was negative; a dilution of 1:100,000 gave a pin-sized reaction; with a dilution of 1:10,000 the reaction was of the size of a nickel and showed marked erythema and infiltration.

The roentgen examination of the chest revealed old calcified tubercle deposits along tracheobronchial nodes.

The histologic examination revealed changes similar to those found in pernio.

The treatment has been restricted to administration of five intravenous injections of cevitamic acid per week. The first injection was given on Oct. 30, 1934. The total has been six doses of 100 mg. each and seven doses of 200 mg. each. After the first two injections the lesions improved both subjectively and objectively.

While the observed improvement may have been a remission due to chance or to factors other than the therapy, the patient herself stated that never before had there been such a striking change during attacks at this time of the year.

DISCUSSION

DR. D. BLOOM: In the last few years I have observed at the Bellevue Hospital a large number of such cases; the appearance of the condition is simultaneous with the advent of cold weather. Most of the patients were young girls who presented the bluish-red plaques on the legs. I consider this eruption as chilblains due to a lack of sufficient protection against cold.

DR. SAMUEL M. PECK: I intend to treat a series of various cutaneous eruptions with cevitamic acid. Since this preparation has become commonly available I have obtained a large supply, and I am especially interested in treating patients who because of sensitivity to certain foods have been deprived for long periods of foods containing cevitamic acid. Since this substance is available I do not hesitate any more in putting a patient on a diet free from vegetables and fruit juices for a relatively long period of time. It has seemed to me that owing to elimination of certain foods because of hypersensitivity, a partial vitamin deficiency which is reflected in the skin actually develops in a number of the patients.

DR. W. GARBE (by invitation): Cevitamic acid in crysal form was used. It could not be sterilized, as the process decreased its efficiency. I began the treatment with 25 mg. and increased the dose to 200 mg. The acid is readily soluble, and 1 cc. or 2 cc. can be given daily. It is also available in tablet form. My co-workers and I have tried it in neurodermatitis and urticaria. The patients with neurodermatitis improved slightly at first and then had a relapse in which marked itching occurred.

DR. ADOLPH ROSTENBERG JR.: It is claimed that some risk is associated with the intravenous administration of cevitamic acid. I understand that no reactions have occurred at the New York Post-Graduate Medical School and Hospital, and the therapy has been used there extensively. As to the technic of administration, in a recent issue of *The Journal of the American Medical Association* (Fisher, B. H.: The Parenteral Administration of Cevitamic Acid (Ascorbic Acid) Solutions, J. A. M. A. **103**:1556 [Nov. 17] 1934) partial neutralization with sodium bicarbonate before administration has been suggested. Vitamin C is probably needed in the body in order to prevent sensitization. When this vitamin is present in adequate amount sensitization of any nature does not develop easily.

THE TREATMENT OF PSORIASIS VULGARIS WITH SHALE OIL. Presented by DR. SAMUEL M. PECK.

This man, aged 28, presents a typical psoriatic eruption of the scalp and arms, of a few months' duration. He will be treated with shale oil.

DISCUSSION

DR. SAMUEL M. PECK: In referring to this therapy I do not wish to give the impression that I have a startlingly new treatment for psoriasis. For two years I have been experimenting with the use of shale oil in the treatment of selected patients with this disease. In my opinion it has helped a number of patients on whom other methods of treatment seem to have failed. Shale oil is a thick tarry oily substance which on standing leaves a gummy residue. The odor reminds one of sulphonated bitumen plus some petroleum product. This substance is partly mineral and partly vegetable. It is obtained as a by-product in certain mines and, I believe, also from some oil wells. Through the cooperation of Dr. Louis Schwartz of the United States Public Health Service, I was able to obtain a number of samples from the Southwest. I found that certain samples of shale oil had absolutely no effect on the psoriatic lesions while others seemed to be efficacious. I have usually advised patients to apply this substance to the lesions in the morning and in the evening. When this is done for a number of weeks the psoriatic lesion gradually yields in some of the cases. I have also found shale oil useful in the treatment of lichenified eczema as it is both keratolytic and antipruritic.

DR. G. J. SPINNER: My co-workers and I attempted to treat psoriasis with shale oil about a year ago, and we had the same experience as Dr. Peck in trying to obtain the material. We sent to the United States Bureau of Mines and were advised that there was no specific form of shale oil and that the samples prepared from shale from various mines were entirely different as to their chemical formulas. The product we used came from Oklahoma. It was tried on two patients and proved a failure in both instances.

DR. THEODORE ROSENTHAL: Shale oil is a tar. The tars are essentially hydrocarbons of various multiples. Sulphonated bitumen is a derivative of shale oil and contains a high percentage of sulphur. Shale oil is found in mines which have large quantities of shale. I should expect the properties of shale oil to be similar to those of sulphonated bitumen.

DR. D. L. SATENSTEIN: I should like to suggest to Dr. Peck that the same procedure be used with other medications and the results compared. Almost anything can be used with surgical plaster and maceration and removal of scales and thickened epidermis be obtained. I suggest that in the treatment of the same patient some lesions be treated with this oil and others with some other preparation and that the results be compared.

MINNESOTA DERMATOLOGICAL SOCIETY

D. D. TURNACLIFF, M.D., *Secretary*

Dec. 7, 1934

HAMILTON MONTGOMERY, M.D., *President*

A CASE FOR DIAGNOSIS. Presented by DR. JOHN BUTLER, Minneapolis.

This married woman, aged 28, says that five weeks ago she noticed a lesion resembling a pin scratch on the chin. The lesion was sharply marginated and became eroded; there was a peripheral spreading of about ½ inch (1.27 cm.) in diameter; there was no apparent infiltration and no pus, but considerable oozing serum which dried on the surface as a thin varnish-like crust was present.

Three weeks later (about two weeks ago) she noticed an enlargement of the sublingual glands. The mass was about the size of a walnut and seemed to be soft and lobulated. It does not seem to have enlarged since it was first noticed.

The first time I saw the patient, about a week ago, she said that she had been applying phenolized petrolatum to the sore. She discontinued the use of antiseptics, and several dark-field examinations as well as an examination of the serum aspirated from the gland were made. No spirochetes were found.

The diagnoses of sporotrichosis, tularemia and isolated chancre-like facial pyodermia have been considered.

DISCUSSION

DR. S. F. SWEITZER, Minneapolis: Dr. Butler asked me to see this patient, and when I saw her a few days ago she had a little eroded lesion on the side of her chin which looked a great deal like a chancre of the parchment type, and under the jaw at least two glands were easily palpated. These glands were painless and freely movable. I do not know of any one who is more expert at finding spirochetes than Dr. Butler, and he has made repeated examinations and has not found any. I was inclined to believe that the lesion is a chancre, but if Dr. Butler cannot find spirochetes I should say that the diagnosis of sclerosis is not correct.

DR. H. E. MICHELSON, Minneapolis: I thought of syphilis and tularemia but could not decide that the condition is either one of these diseases. Opposed to the diagnosis of syphilis are the submental adenitis and the lack of massive enlargement of the submaxillary gland. The patient does not seem to be sick enough to justify a diagnosis of tularemia.

DR. PAUL A. O'LEARY, Rochester: In addition to the diagnostic possibilities already mentioned, I considered also a possibility of tuberculous inoculation. However, apple jelly tubercles could not be demonstrated in the cutaneous nodules, even with the aid of a diascope, and the bubo is harder than would be expected after five or six weeks' duration. Examination for tubercle bacilli in smears made from material from the nodule as well as from that aspirated from the bubo should be carried out. If this case is proved to be one of tuberculous inoculation, it represents my concept of the primary complex of tuberculosis. I mention this because of the discussion in regard to this complex which the members had when the patient with the tuberculous ulcer of the ankle resembling scrofuloderma was presented by Dr. Michelson several months ago as having a primary complex of tuberculosis (ARCH. DERMAT. & SYPH. **30**:893 [Dec.] 1934). The evidence of direct inoculation with the development of a tuberculous chancre and a bubo is demonstrated in the patient presented this evening and warrants the designation of primary complex, while in the type of case with which I am comparing this one the condition is more suggestive to me of a secondary complex in the sense that the ulcer is the result of transmission of the tubercle bacilli to the ankle from some primary focus within the body.

DR. HAMILTON MONTGOMERY, Rochester: Dr. Butler's case reminds me of that of a 10 year old child who apparently had a furuncle on the cheek and a satellite gland in the same location as the glandular mass shown by Dr. Butler's patient. The lesion on the cheek was treated with ammoniated mercury ointment and showed improvement over a period of several weeks. The gland remained about the same size. When the gland became fluctuant a specimen for biopsy revealed the picture of tuberculosis.

LYMPHOGRANULOMA INGUINALE. Presented by DR. JOHN F. MADDEN, St. Paul.

A. M., a laborer aged 28, states that he noticed a small pinhead-sized superficial erosion on the prepuce about the last week in October 1934. This lesion was painless, exuded a slight amount of serum and healed in about ten days. The appearance of the penile lesion was followed in about four or five days by that of lymphadenitis on the right side. The glands were painful and matted together, forming a mass about the size of an egg. In two weeks the mass became fluctuant. It was incised, and a small amount of pus drained.

I was unable to find Ducrey bacilli and repeated dark-field examinations for spirochetes gave negative results. The Wassermann test of the blood also was negative on several occasions.

All the Frei tests which were made gave strongly positive results. The Frei test was made on two normal persons as a control and gave negative results in both instances.

NOTE.—On Dec. 24, 1934, the penile lesion had disappeared and the glands were still draining, although they were somewhat smaller and not as painful.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester: At the recent meeting of the Dermatological Conference of the Mississippi Valley in San Antonio, Texas (ARCH. DERMAT. & SYPH. **31**:577 [April] 1935), several patients with lymphogranuloma were shown in whom the therapeutic use of the Frei antigen had produced a rapid involution of the buboes. My co-workers and I have had experience which also indicates that the antigen has a definite therapeutic value in such cases.

JOHN F. MADDEN, St. Paul: I think that this is the first case of lymphogranuloma inguinale that has been reported from St. Paul. The first Frei test was made shortly after the penile lesion appeared, and although the amount of antigen used has been the same, the reaction becomes more pronounced at each test.

DR. S. E. SWEITZER, Minneapolis: My co-workers and I have found that instead of experiencing a beneficial effect, the patients did not obtain any benefit from the antigen; in one case the lesion increased tremendously in size. We finally treated the patient with diathermy, and that cleared up the condition.

DISCOLORATION OF THE TEETH. Presented by DR. S. E. SWEITZER, Minneapolis.

This woman, aged 24, presents a mottled pigmentation of the enamel of the permanent teeth. She was born and raised near Brittin, S. D.

This peculiar condition, which affects the enamel of the permanent teeth, was first described by Black in 1916. It involves the developing enamel in persons living in certain districts where the fluorine content of the drinking water is abnormally high. Ordinarily the fluorine content is 1 part per million, but in certain localities in Idaho, Colorado, Arizona and North and South Dakota the fluorine content is as high as 12 parts per million.

DISCUSSION

DR. CARL W. LAYMON, Minneapolis (by invitation): This type of mottling of the enamel is due to the presence of an abnormally high content of fluorine in the drinking water. The home of this patient was near Brittin, S. D., where the fluorine content of the water is 12 parts per million. Other locations where mottling of the enamel is prevalent are Oakley, Idaho; Lidgerwood, N. D.; Colorado Springs, Colo., and St. David, Ariz. It has been shown that deficient diet is not the cause of the condition, and the discoloration has been produced in dogs by the addition of fluorine to the drinking water.

DR. JOHN F. MALDEN, St. Paul: This patient states that all the children who went to school with her had a similar discoloration of the teeth. How long does one have to drink the water before the first sign is noted on the teeth?

DR. CARL W. LAYMON, Minneapolis (by invitation): The temporary teeth are rarely affected, and when the condition is present before the permanent teeth erupts, it affects only the molars.

DR. JOHN BUTLER, Minneapolis: It would seem as though the condition would not appear when the permanent teeth are developed.

DR. CARL W. LAYMON, Minneapolis (by invitation): Only the enamel which is developed during residence in the involved district is affected.

Dr. D. D. Turnacliff, Minneapolis: Is this condition present on the teeth as they erupt?

Dr. Carl W. Laymon, Minneapolis (by invitation): Yes, it is.

Dr. S. E. Sweitzer, Minneapolis: Some of these communities have changed their water supply, and since then the children have good teeth.

Scleroderma of the Legs. Presented by Dr. E. Z. Shapiro, Duluth.

This widow, aged 62, has had an eruption for the past six years. The lesions are located on the legs between the ankle and the knee, encircling the legs all the way around. The skin appears smooth and shiny and is dark brownish red. The skin feels tense and cannot be picked up with the fingers.

A biopsy showed typical atrophy of the entire malpighian layer with a dense infiltration of fibrous tissue.

No treatment has been instituted.

DISCUSSION

Dr. Paul A. O'Leary, Rochester: My co-workers and I have treated five patients with generalized scleroderma with the Kettering-Simpson vapothermy unit, in which the patient's temperature is readily elevated to 105 or 106 F. In two of the patients the affected areas have softened considerably, the remaining three have derived no benefit from the treatment. We are at present endeavoring to determine a means of selecting beforehand the patient in whom response to the therapy may be expected.

Sarcoid of Boeck. Presented by Dr. S. E. Sweitzer, Minneapolis.

This woman, aged 50, presents on the lower extremities several oval plaques which are movable over the underlying structures. The plaques are firm and reddish. Beneath the surface sheen, small areas of delicate telangiectasia may be noted. The larger lesion on the anterior surface of the right leg measures 3 by 3 cm. in diameter. There are two similar, though smaller, lesions on the anterior surface of the left leg. None of the lesions has involuted.

The lesions have been present for five years. There have been no associated constitutional symptoms, except a slight pruritus when the patient exerts herself during the warm seasons. There is no local tenderness on palpation.

Roentgenograms of the chest showed no abnormalities. Studies of the blood and the Wassermann test gave negative results. The Mantoux reaction was positive with a concentration of 1:10,000. Biopsy specimens are shown.

DISCUSSION

Dr. John Butler, Minneapolis: I do not think that the condition is sarcoid; I think that the plaques are healed syphilitic lesions.

Dr. L. A. Winer, Minneapolis: When this woman came into the clinic about four months ago the possibility of old syphilitic lesions and of sarcoid of Boeck was considered. The first two Wassermann tests gave negative results. A biopsy was made, and in my opinion the appearance of the specimen suggested sarcoid rather than syphilis. Under treatment with bismuth the lesions have receded markedly. When the patient was first seen the large lesion was elevated, felt thick and velvety and was freely movable on the underlying tissues. Under treatment with a preparation of bismuth (twelve or fourteen injections) the lesion has become firm, tense and sunken. There is room for considerable discussion regarding this case, but I still believe that the condition is sarcoid of Boeck.

Dr. John Butler, Minneapolis: The eruption is superficial. In my opinion a superficial scar with stippling indicates a healed syphilitic lesion, despite the negative Wassermann reaction.

Dr. L. A. Winer, Minneapolis: The specimen for biopsy was taken the first day the patient came to the clinic.

DR. H. E. MICHELSON, Minneapolis: It is difficult to make a decision about this lesion. Although the microscopic picture was somewhat suggestive of sarcoid, it showed so many plasma cells that I could not agree with that diagnosis. It does not seem possible that a superficial plaque of this sort could be due to syphilis and show no changes for five years, even though there is a slight central atrophy. To entertain the thought of plaquelike tuberculid one must first decide what type of tuberculosis one is willing to put in the tuberculid class. For my part I consider the tuberculid a labile form of tuberculosis. Any lesion that has been present for five years could not be called a tuberculid. There is no evidence of lupus vulgaris; hence I cannot make a diagnosis at the present time.

DR. S. E. SWEITZER, Minneapolis: This patient has been under observation for several months. She has had a number of elevated and flat lesions that did not look at all like lesions of syphilis; they looked more like tuberculid en plaque. She must have had six or eight lesions. They leave slightly depressed areas. I thought the eruption looked more like tuberculid en plaque. It certainly did not look like syphilis when the patient was first seen.

DR. HAMILTON MONTGOMERY, Rochester: The question of syphilis as an etiologic factor in certain types of sarcoid or the ability of certain cutaneous syphilids to imitate the clinical and histopathologic picture of sarcoid has been the subject of considerable discussion in the French literature for many years. Dr. Michelson and his associates have made special studies regarding tuberculoid types of reactions in various forms of syphilis, and if he is unwilling to distinguish between tuberculosis and syphilis in this case, I certainly am not willing to do so. I believe that there is an attempt to classify and subdivide tuberculous lesions of the skin too closely. Various forms of hematogenous tuberculosis may at times simulate one another. This case reminds me of a group of cases that Nomland recently reported under the title "Hematogenous Cutaneous Tuberculosis (Sarcoid) in Negroes" (Nomland, Reuben: ARCH. DERMAT. & SYPH. **30**:59 [July] 1934). The patient should be observed further before a definite diagnosis is made.

DR. PAUL A. O'LEARY, Rochester: If the roentgenograms showed evidence of fibrocystic disease in the swollen fingers and if infiltration were found in the lungs, further evidence would be at hand in support of the diagnosis of sarcoid.

DR. CARL W. LAYMON, Minneapolis (by invitation): French authors have recently expressed the opinion that sarcoid is the expression of various infections, the great majority of which are tuberculous. Syphilis, however, can rarely produce lesions which clinically and histologically resemble tuberculous sarcoids.

COLLOID MILIUM. Presented by DR. H. E. MICHELSON, Minneapolis.

H. S., a woman aged 79, has noticed changes in the skin of the face for the past two years. There has been no definite progression since the onset of the condition.

There are multiple pinpoint ivory-colored soft papules localized chiefly on the forehead and, to a lesser extent, on the nose and sides of the face. The rest of the body is not affected. Puncture of the lesions yielded a glary mucoid material. The patient has received roentgen therapy for a basal cell carcinoma of the left side of the nose.

A biopsy specimen is shown.

DISCUSSION

DR. CARL W. LAYMON, Minneapolis (by invitation): About two years ago I observed a case of pseudoxanthoma elasticum and considered colloid milium in the differential diagnosis. The lesions in the former condition occur most frequently over the body folds, are translucent or waxy in appearance and emit no secretion when punctured. The lesions in colloid milium, which is also known as pseudocolloid milium or miliary colloidoma, are superficial, may resemble vesicles, are usually located on the face and yield a mucus-like material when punctured. In pseudoxanthoma elasticum the chief histologic changes occur in the elastic tissue, while in colloid milium the most severe involvement is in the collagenous tissue.

ELEPHANTIASIS. Presented by DR. H. E. MICHELSON, Minneapolis.

B. H., a woman, aged 51, has noticed enlargement of the legs since 1925. At that time the legs were larger than they are at present. An ulcer of the right leg also appeared in 1925 and has healed and broken down several times since. Red areas have been present on the calf of the left leg for six years. The patient has had thirteen pregnancies, seven children are living and well, one child is dead and there were five miscarriages. The youngest child is 12 years old.

Both legs below the knees are enormously enlarged. Extraordinarily large varicosities are present on both legs and extend to the inguinal region. There is pitting on pressure, but it is surprisingly slight in view of the size of the limbs. There is a round ulcer 4 cm. in diameter over the right tibia midway between the knee and the ankle joint. The left calf, both anteriorly and posteriorly, presents fairly sharply demarcated plaques which are dull red, raised, and painless on pressure.

A biopsy specimen is shown.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester: I have seen two cases of elephantiasis in the last couple of months; in one case the condition was limited to one arm and in another, to one leg. In both instances the trouble was due to squamous cell epithelioma which had spread along the lymphatics, blocking them and thus resulting in the picture of elephantiasis.

CALCINOSIS CUTIS. Presented by DR. H. E. MICHELSON, Minneapolis.

E. L., a woman aged 51, has suffered from cutaneous trouble for twenty years. The lesions first appeared as "shots" beneath the skin. These were movable and grew to the size of a pea. For the past ten years the lesions have been larger and more numerous but have remained localized in the upper and lower extremities. The subcutaneous deposits have never broken through to the surface. Itching has been severe at times. The disease as a whole has gradually become worse.

There are subcutaneous firm tumors which can be palpated beneath the skin of the arms and thighs. The lesions vary in size and are covered and fixed to the overlying erythematous skin. The Wassermann reaction was negative. The urine was normal. The routine examinations of the blood showed no significant changes: The blood urea nitrogen was 12.9 mg. per hundred cubic centimeters; the calcium, 8.4 mg.; the phosphorus, 3.9 mg., and the uric acid, 1.8 mg. The basal metabolic rate was —4.

Roentgenograms of the arms and legs showed multiple areas of calcification in the subcutaneous tissues. Biopsy specimens are shown.

EPITHELIOMA OF THE PENIS. Presented by DR. S. E. SWEITZER, Minneapolis.

This man, aged 58, has a lesion on the dorsum of the penis about the coronal sulcus, which measures 2 by 2.5 cm. in diameter. The lesion has rolled irregular edges, and there is moderate induration. The patient states that the lesion has been present for four months and first appeared after trauma by clothes. There is an inguinal lymphadenitis with palpable nodes. The biopsy showed epithelioma, grade 1.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester: The plaquelike lesion with the papillomatous area presented by this patient may be interpreted as an erythroplasia of Queyrat. I believe, however, that this is simply a variant of leukoplakia with erythematous and malignant changes. Histologically the picture is that of a squamous cell epithelioma, grade 1, with changes like those in Bowen's disease, which in many places are already beginning to invade the deeper layers of tissue. There is no reason for calling these lesions manifestations of Bowen's disease simply because the histologic picture may resemble that described by Bowen. It has been my experience that many squamous cell epitheliomas of the so-called mucous mem-

branes show changes like those in Bowen's disease consisting of marked keratinization of individual cells, amitotic as well as mitotic cell division, and clumping of cells to form epidermal giant cells.

Dr. Elmer Rusten, Minneapolis (by invitation): This case presents several interesting features well illustrated in an article by Ngai (Ngai, S. K.: Etiological and Pathological Aspects of Squamous-Cell Carcinoma of the Penis Among Chinese, Am. J. Cancer **19**:259 [Oct.] 1933). He reported a group of one hundred and seven cases of carcinoma of the penis. In 10 per cent of the cases the disease resembled leukoplakia; in 10 per cent the condition was infiltrative; in 50 per cent, papillary, and in 29 per cent, nodular. The results of microscopic examination in these cases agree fairly well with the results reported by other authors who have studied cases of carcinoma of the penis. According to Broder's classification, 51 per cent of the cases which formed the basis of Ngai's report were of grade 1; 21 per cent, of grade 2; 15 per cent, of grade 3, and 11 per cent, of grade 4. These figures confirm the observation frequently made that epithelioma of the penis metastasizes late. Of the cases in which the inguinal nodes were examined, less than one-half showed evidence of metastasis. It is interesting also to note the high incidence of carcinoma of the penis in patients who are not circumcised, and the evidence of the relation of circumcision to that condition is also corroborated in the low incidence of such cases among Jews.

Acne Rosacea with Tuberculoid Features. Presented by Dr. S. E. Sweitzer, Minneapolis.

This woman, aged 41, states that the eruption appeared first on the right side of the face ten months ago later involved the left side of the face. The eruption consisted of papules, pustules and areas showing dilatation of the vessels. At present practically all the lesions have healed.

The reaction to the Mantoux test was 3 plus; roentgenograms of the chest showed no evidence of pathologic changes. The histologic picture was surprisingly like that of tuberculosis.

DISCUSSION

Dr. H. E. Michelson, Minneapolis: There is no doubt that there is a rosacea-like tuberculid, and those of the members who have had an opportunity to observe this rare form of tuberculosis realize that it is a highly resistant form, which is, I believe, more closely related to miliary lupus than to acnitis. I think the term rosacea-like tuberculid is used too freely. Recently Dr. Wile told me he was reporting some cases of that disease, and I note that an article on the subject is being prepared by McKee. After reading Lewandowski's original contribution and subsequent reports of cases I fully decided that the definite diagnosis of rosacea-like tuberculid has been made too often. I was glad to hear Dr. Freeman speak of a tuberculid-like rosacea, a diagnosis which probably covers quite a number of cases.

Dr. S. E. Sweitzer, Minneapolis: This is an interesting subject. Dermatologist's have tried to make biopsies in these cases, but a number of patients refuse to submit to removal of tissue for biopsy. I think it would be a good idea to make a biopsy in all these cases.

Dr. John F. Madden, St. Paul: My co-workers and I made biopsies in two or three cases of acne rosacea and found a tuberculoid structure in all the sections. This alone cannot be a differential point between acne rosacea and tuberculid.

A Case for Diagnosis: Lupus Erythematosus? Hydroa Aestivale? Dermatitis Herpetiformis? Presented by Dr. H. E. Michelson, Minneapolis.

M. B., a woman aged 39, states that her eruption appeared eight years ago on the face, V-area of the neck and extensor surfaces of the arms. It has spread to the back within the past six months. The lesions have usually appeared in

May and involuted in December, reappearing again in the spring. Exposure to the sun has definitely aggravated the eruption. The eruption has always been extremely pruritic.

There are lesions on the face, chest, back and extensor surfaces of the arms. The earliest lesions appeared to be deep red papules which enlarged and coalesced to form plaques, a few of which showed slight central scaling. Many of the papules are superficially excoriated. There is no follicular plugging and no atrophy. The patient also has exophthalmic goiter. The basal metabolic rate was +47 in August 1934. A biopsy specimen is shown.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I think that the condition is lupus erythematosus.

DR. JOHN BUTLER, Minneapolis: I think that it is lupus erythematosus of the subacute type.

DR. S. E. SWEITZER, Minneapolis: I think that it is due to sensitization to light.

DR. JOHN F. MADDEN, St. Paul: This patient has had many lesions on the covered portion of the body, especially over the shoulders and on the arms. Scarring and pigmentation are present at the sites of these lesions. Both the hands and the face are free from the eruption.

DR. HAMILTON MONTGOMERY, Rochester: The biopsy specimen in this case shows none of the epidermal changes seen in lupus erythematosus or dermatitis herpetiformis, and the areas of parakeratosis argue against the former diagnosis. It is true that there is a dense infiltration about the dermal appendages, and this is consistent with sensitization to light as well as with many of the other conditions mentioned. I think it would be worth while to make another biopsy.

PITYRIASIS RUBRA PILARIS. Presented by DR. S. E. SWEITZER, Minneapolis.

This woman, aged 23, states that her lesions have been present as long as she can remember. However, there are periods of exacerbation and of improvement. There is only a minimum of subjective symptoms, consisting of dryness and a feeling of tightness of the skin. The father and three brothers have a similar cutaneous disorder.

The patient presents many fine acuminate papules about the openings of the hair follicles, with superimposed fine grayish scales. The eruption is most marked over the extremities and on the sides of the neck. The papules have a rough feel when palpated, and the cutaneous markings are intensified. A biopsy specimen is shown.

ACNE ROSACEA WITH LESIONS ON THE CORNEA AND SCLERA. Presented by DR. S. E. SWEITZER, Minneapolis.

This woman, aged 41, presented lesions of acne rosacea on the face and bridge of the nose, which have been present for several months. Recently a lesion developed on the cornea. The patient is being treated for corneal ulcers under the supervision of the ophthalmologic department.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: Cranston Low of Edinburgh was the first one to call this subject to the attention of dermatologists. That was in 1921. Many articles had been written before, and a few have been written since. The disease is sometimes classified as a true keratitis and at other times as a phlyctenular conjunctivitis. It has been my experience that the ocular condition is difficult to heal and that flare-ups frequently occur. The cure of the rosacea, to be sure, improves the ocular condition.

DR. PAUL A. O'LEARY, Rochester: The ophthalmologists at the Mayo Clinic recognize keratitis as a manifestation of acne rosacea which they call rosacea keratitis, and they refer patients with such conditions to the dermatologic depart-

ment for treatment, as they believe that elimination of the rosacea is essential to the treatment of the keratitis. The patient presented has the type of rosacea which I have found shows excellent response to the Ayres treatment (Ayres, Samuel Jr., and Anderson, Nelson P.: Demodex Folliculorum: Its Rôle in the Etiology of Acne Rosacea, ARCH. DERMAT. & SYPH. **25**:89 [Jan.] 1932).

CARCINOMA OF THE FACE. Presented by DR. S. E. SWEITZER, Minneapolis.

This man, aged 72, has a lesion on the right side of the face which has been present for one year. This lesion has recently grown considerably in size; at present it measures 2 by 1.5 cm. and is slightly pedunculated. It is composed of friable tissue and bleeds easily. Biopsy showed basal cell carcinoma.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester: At a recent meeting of a dermatologic society I heard two prominent dermatologists, both of whom have for many years been ardent exponents of the use of roentgen rays and radium, decry the use of these agents in the treatment of malignant diseases of the skin. More than ten years ago dermatologists agreed that it was unwise to treat an epithelioma by radiotherapy without first knowing the type and grade of the malignancy. Accordingly, nowadays a biopsy is made on all such lesions and the growth is then destroyed with cautery; depending on the type and grade of the malignancy, dissection of the adjacent glands, followed by roentgen or radium therapy, is performed when indicated. The low grade epitheliomas respond readily to roentgen or radium therapy, but those of a higher degree of malignancy and those of the basal squamous cell type are resistant to these agents. At the clinic there are many more failures than successes resulting from roentgen and radium therapy, and experience with the higher grades of malignancy demonstrates the superiority of cautery destruction over roentgen and radium therapy. The panacea for the treatment of epitheliomas has not been described; hence in the severe grades of malignancy it is necessary to use all the worthwhile therapeutic agents available.

DR. S. E. SWEITZER, Minneapolis: I think this discussion is extremely interesting. There are many cases of cancer of the skin, and in most of them treatment with roentgen rays and radium is used; probably 97 per cent of the patients with malignant diseases of the skin are so treated and are cured.

DR. H. E. MICHELSON, Minneapolis: For a number of years in discussing cancer of the skin I have prefaced my remarks, with the statement that until one made a biopsy one could not discuss learnedly either the diagnosis or the therapy. There is no question that much of the abuse in the use of radium is due to the fact that the clinical diagnosis is not sufficient to define accurately the type of the lesion under consideration, and therefore a dosage given to what is clinically diagnosed as a basal cell epithelioma may fail to produce results because the lesion is a mixed or squamous cell epithelioma. The consideration of the lesion as to the anatomic location, duration, size, morphologic type and microscopic diagnosis is what makes for a correct choice in therapy. One cannot dismiss the use of roentgen and radium therapy with a statement that such treatment is unsuited for cancer of the skin, for in many patients treated by this means perfect results are obtained even though the lesions are of the squamous cell type. On the other hand, the best surgical excision does not always bring about a cure. In the Cancer Institute no one definite method of treatment is employed, but irradiation, surgical excision, and desiccation are all considered and used when indicated.

DR. CARL W. LAYMON, Minneapolis (by invitation): It is difficult to discuss such a subject as cutaneous epithelioma unless there is a definite understanding as to the types that are included, their location, etc. Most of the recurrences following radiation therapy in uncomplicated malignant diseases of the skin which have not metastasized result from inadequate dosage.

DR. HAMILTON MONTGOMERY, Rochester: I think that the divergence in views with regard to radiotherapy as against surgical excision, desiccation or diathermy

for the treatment of epithelioma is due in part to the difference in the types of lesions encountered. The dermatologist usually sees the smaller lesions, and if a specimen for biopsy were taken in all these cases, the larger percentage of the lesions would prove to be basal cell epithelioma. In surgical practice, however, the reverse is true, and the majority of the lesions encountered are squamous cell epithelioma. Ordinary basal cell epithelioma (rodent ulcer) responds to radiotherapy in the majority of instances; but, as I stated, 20 per cent of the lesions diagnosed as such clinically prove on histologic examination to be basal-squamous or squamous cell epithelioma. Whereas it is possible to clear up some of the latter lesions by more intensive radiotherapy, the roentgen or radium treatments must be given in such large doses that there is no longer any selective action, and hence that type of treatment offers no particular advantage over destruction by cautery, diathermy, surgical excision or a combination of these methods. Moreover, there is the disadvantage that if radium or roentgen therapy fails to bring about a cure, subsequent surgical intervention is rendered more difficult because of sclerosis of the tissues and changes in the vessels. The lesions of superficial epitheliomatosis are usually of the basal cell type but are not amenable to roentgen therapy, presumably because of their slow growth. I have seen cases in which lesions of superficial epitheliomatosis have recurred in areas of actinodermatitis. Epithelioma arising from arsenical keratoses is especially resistant to radiotherapy, as is to be expected, as the early histologic changes in the type of epithelioma due to arsenic simulate those seen in many instances of early epithelioma due to roentgen rays or radium. I especially urge against treatment of leukoplakic vulvitis by radiotherapy, which may be given to the point of clearing up the leukoplakia or causing involution of an early squamous cell epithelioma, but such treatment often results in a residual area of actinodermatitis which is extremely painful and which, in turn, may result in epitheliomatous change.

Book Reviews

Modern Clinical Syphilology: Diagnosis—Treatment—Case Studies. By John H. Stokes. Second edition. Price, $12. Pp. 1,399, with 973 illustrations. Philadelphia: W. B. Saunders Company, 1934.

The appearance of this new edition attests the popularity that Stokes' work has attained. The features which gave the first edition individuality were especially the systematic way in which the subject was presented; the introduction of differential tables, particularly of diagnosis, which cleared and emphasized the points that were considered in each table; the minute attention given to technic and detail in the handling of the cases, and the intensive thoroughness of the whole work. The book has been thoroughly revised, but fortunately these characteristics have not been lost. The work remains, on the whole, perhaps the most intensive study of syphilis that has been made, at least in English. Fifteen of the original twenty-three chapters have been rewritten. A valuable chapter has been added on relapses and progression, which, in the way in which the subject has been brought together, is an addition to works of this sort. Other outstanding chapters are those on immunity, cardiovascular syphilis and familial and prenatal syphilis. As formerly, Stokes has emphasized the importance of treating the syphilitic patient as a person sick with syphilis and not a "case," and he has retained his valuable section on the examination of patients. For the person who does not frequently see syphilis it would be a good plan to keep Stokes' outline of examination at hand for reference. The work is, of course, up to date; the reviewer knows no new knowledge of the subject which is not included. Stokes has used freely the assistance of collaborators who, the reviewer believes, in all instances are associates in Stokes' clinic, and he characteristically gives them generous credit. But the work is Stokes'—a product which has been fused into a well balanced whole by one person with an extraordinarily able and active mind and with a background of wide scholarship who has chosen the entire subject of syphilis for his domain.

Directory of Dermatologic Societies *

INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY

American Secretary: Dr. Howard Fox, 140 E. 54th St., New York.
Place: Budapest, Hungary. Time: Sept. 15-21, 1935.

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY (CANADIAN BRANCH)

H. A. Dixon, President, Medical Arts Bldg., Toronto, Ont.
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg., Toronto, Ont.
Place: Toronto, Ont. Time: May 1936.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

Henry MacCormac, President, 23, Wimpole St., London, W. 1.
R. T. Brain, Secretary, 132, Harley St., London, W. 1.

NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Jeffrey C. Michael, Chairman, 1215 Walker Ave., Houston, Texas.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.
Place: Atlantic City. Time: June 10-14, 1935.

AMERICAN DERMATOLOGICAL ASSOCIATION

Charles M. Williams, President, 114 E. 54th St., New York.
W. H. Guy, Secretary, 500 Penn Ave., Pittsburgh.

SECTIONAL DERMATOLOGIC SOCIETIES

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Joseph E. Gately, President, 1129 Calvert St., Baltimore.
Joseph V. Kennedy, Secretary, 1835 Eye St., Washington, D. C.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

John R. Schermerhorn, President, 1225 Union St., Schenectady.
L. de Mello, Secretary-Treasurer, Medical Arts Bldg., Syracuse.

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cincinnati. Time: 1935.

IOWA AND WESTERN ILLINOIS DERMATOLOGICAL ASSOCIATION

J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First Natonal Bank Bldg., Davenport, Iowa.
Place: Iowa City. Time: Oct. 15, 1935.

NEW ENGLAND DERMATOLOGICAL SOCIETY

William P. Boardman, President, 388 Marlborough St., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

J. W. Roussel, Chairman, 150 Baronne St., New Orleans.
Cornelius F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Ernest K. Stratton, Chairman, 490 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

Florida Society of Dermatology and Syphilology

Chairman for each meeting is elected from city in which meeting is held.
J. J. Saxton, Secretary, 205 Zack St., Tampa.
Place: Jacksonville. Time: June 1935.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. MacKee, Chairman, 200 W. 59th St., New York.
Lopo de Mello, Secretary, Medical Arts Bldg., Syracuse.

Medical Society of the State of Pennsylvania Section on Dermatology

Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
Fred M. Jacob, Secretary, 7026 Jenkins Arcade Bldg., Pittsburgh.

Michigan State Medical Society, Section on Dermatology and Syphilology

A. R. Woodburne, Chairman, 26 Sheldon Ave., Grand Rapids.
G. Warren Hyde, Secretary, 2501 W. Grand Blvd., Detroit.

Minnesota Dermatological Society

Hamilton Montgomery, President, Mayo Clinic, Rochester.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma State Dermatological Society

C. L. Brundage, President, 1200 N. Walker St., Oklahoma City.
M. M. Wickham, Secretary, 716 W. Symmes St., Norman.

Texas Dermatological Society

J. C. Michael, President, 1215 Walker Ave., Houston.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Austin.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Louis Chargin, Chairman, 1 W. 85th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Jacob Skeer, President, 272 E. 19th St., Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Albert R. McFarland, President, 315 Alexander St., Rochester, N. Y.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

CHICAGO DERMATOLOGICAL SOCIETY

William A. Pusey, President, 7 W. Madison St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

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CLEVELAND DERMATOLOGICAL SOCIETY

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E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

DETROIT DERMATOLOGICAL SOCIETY

Clyde K. Hasley, President, 1553 Woodward Ave., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

LOS ANGELES DERMATOLOGICAL SOCIETY

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Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles.

MANHATTAN DERMATOLOGIC SOCIETY

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

MONTREAL DERMATOLOGICAL SOCIETY

Alberic Marin, President, 1414 Drummond St., Montreal, Canada.
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NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

Max Scheer, Chairman, 509 Madison Ave., New York.
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NEW YORK DERMATOLOGICAL SOCIETY

R. H. Rulison, Chairman, 145 E. 54th St., New York.
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OMAHA DERMATOLOGICAL SOCIETY

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Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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Vaughn C. Garner, Secretary, Greene and Coulter Sts., Philadelphia.

PITTSBURGH DERMATOLOGICAL SOCIETY

Bernhard A. Goldmann, President, Jenkins Arcade, Pittsburgh.
J. Cavanaugh, Secretary, 28 Market St., Youngstown, Ohio.

ST. LOUIS DERMATOLOGICAL SOCIETY

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M. F. Engman Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis

SAN FRANCISCO DERMATOLOGICAL SOCIETY

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